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THE TREATMENT OF PERNICIOUS VOMITING OF PREGNANCY.*

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This report concerns the treatment of hypermesis gravidarum in 225 consecutive cases from the public wards of the Boston Lying-in Hospital. Patients beyond the twentieth week of gestation were excluded because excessive vomiting later in pregnancy is often a symptom of preeclampsia rather than of hyperemesis gravidarum. This series embraces no mild cases as we do not admit them to the hospital. In 122 instances, or 54.2 per cent, the vomiting had lasted over a month, and 152 cases, or 67.4 per cent, were referred by outside physicians or other hospitals after unsuccessful attempts at treatment. The purpose of this paper is to call attention to certain improvements in treatment which, in the past six years, have enabled us to reduce our incidence of therapeutic abortion from 17.3 per cent to 2.6 per cent, and our mortality from 5.5 per cent to zero. Before explaining, however, how these results have been achieved, it may be advantageous to review some of the facts regarding the etiology, pathology, symptomatology, and diagnosis which a study of this size has revealed, as well as to deal briefly, in its proper place, with some current theories concerning why some women in early pregnancy vomit so much.

ETIOLOGY

From January 1, 1928 to January 1, 1940, a period of twelve years, women with 39,724 pregnancies were admitted to the hospital or treated in the out-patient department, and of these, 225, or 1 in 176, entered because of pernicious vomiting. It is striking however, that only 73, or 1 in 544, were patients that had registered for care in our clinic, and that the remainder, sent in as emergency cases, had been in the hands of private physicians, and hence came from a higher economic stratum. This fact has an apparent bearing upon the frequency of hyperemesis gravidarum. All of our registered patients are in restricted financial circumstances. No patients may register for care at our hospital, which is a semi-charitable institution, unless the family income is below a small set figure. Many of them are poor and the families of many are on relief. Moreover, our registered patients are almost without exception hard working, sensible women who are so occupied with the demands of housekeeping that they will submit to no illness unless it incapacitates them.

Contrary to the usual opinion that pernicious vomiting occurs more frequently in primigravidae, we found that 61.3 per cent of our patients had been pregnant before. This proportion agrees with our usual ratio of multigravidae, which is about 60.0 per cent of the total. Of the 138 multigravidae affected, seventy, or 50.7 per cent, had vomited excessively in one or more previous pregnancies and ten of them had been sufficiently sick to require therapeutic abortion once, two twice, and one five times. Age had no bearing upon the incidence of the condition as most cases occurred during the years of greatest fecundity. (Fig. 1). Figure 2, showing the period of gestation at which each was admitted, indicates that the greatest number entered between the sixth and twelfth weeks. One of our patients had a twin pregnancy and one triplets.

There have been many attempts to link pernicious vomiting to preeclampsia. In opposition to this point of view I wish to remind you that not only do these diseases occur at different periods of pregnancy, but that the general signs and symptoms of each in no way resemble each other; nor when they die, do their organs show the same changes. Moreover, our pa-

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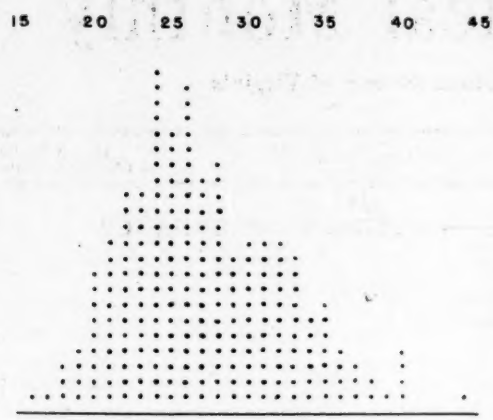

Fig. 1.—Age.

tients with pernicious vomiting showed later in pregnancy no more tendency to develop preeclampsia than did the others in the clinic; the ratio in their case was 1:22.5, and the general ratio is 1:21.

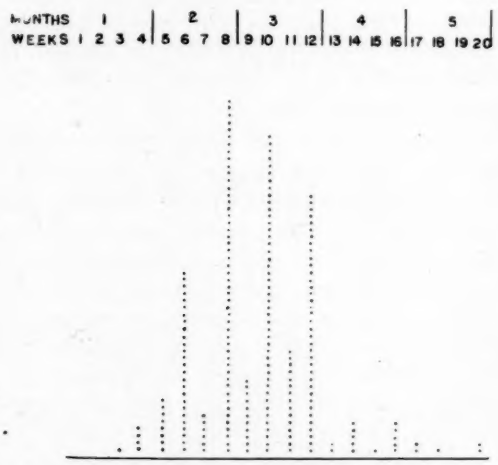

Fig. 2.—Period of gestation at hospital admission.

PATHOLOGY

Stone[1] in 1903, Ewing[2] in 1905 and Williams[3] in 1906 described what they believed to be characteristic lesions of the liver in women who had died of pernicious vomiting. There was necrosis of the central portions of the lobules without involvement of the periphery. Since this picture also occurs in acute yellow atrophy of the liver, it is reasonable to suppose that these patients may have died of that condition rather than from pernicious vomiting. This description, first given wide circulation by Williams as distinctive of hyperemesis gravidarum, has been, and still is being copied in some later textbooks, with no attempt made by their authors to corroborate or to disprove it, either by their own investigations or by the perusal of the more recent literature. For the past thirty years, however, all pathological reports have shown the hepatic change to be the same fatty degeneration that follows extreme starvation. We obtained autopsies in five of our six patients that died and in each case found fatty degeneration of the liver; in no instance did we see the necrotic changes reported by the earlier writers. The conditions in the kidneys were less uniform. Damage to the convoluted tubules, shown by cloudy swelling or fatty degeneration, was found four times. In one case there was swelling of the glomeruli, accompanied by ischemia and hyaline thrombosis, as is present in eclampsia. One case had chronic pyelitis. In all five instances the suprarenal glands were normal.

PATHOGENESIS

In 1769, Robert Johnson,[4] who wrote learnedly upon the subject, attributed the "retchings, loathings and vomitings" with which pregnant women are afflicted, to various causes, but chiefly to retention of the menses which, collecting in the body, caused engorgement of the vessels of the stomach. In the 170 years that have elapsed since then the minds of medical men have not been idle, for with the passage of time and the increase in knowledge, their ideas, though less fantastic, have been no less fertile. Those prodigies of medicine, the sex hormones, have inspired the speculative to new and greater heights of supposition. What could be more alluring than to assume that in the vomiting of pregnancy there must be some derangement of the internal secretions which control the reproductive function?

As long ago as 1916 J. C. Hirst[5] advanced the theory that since the nausea and vomiting of pregnancy occurred when the corpus luteum was growing, an insufficient secretion of progesterone might be its cause. He gave an extract of this structure by intramuscular and intravenous injections and was satisfied with the results, although those who repeated his work found no such beneficial effect. Until 1937, when Venning and Browne[6] isolated sodium pregnandiol glucoronamide, the excretion product of progesterone, there was no accurate method known whereby one could assay the amount of this hormone

that left the body in the urine; nor to my knowledge, although it offers a promising field for investigation, has there been any publication to indicate whether its quantity in pernicious vomiting is decreased, increased, or unchanged. If deficient progesterone secretion produces pernicious vomiting and if it also, as some believe, causes abortion, one would expect these conditions to go hand in hand. On the contrary, only six of our 225 cases miscarried—a frequency of only one in 37.5 cases, as contrasted with the usual expectancy in pregnancy of one in every five or six.

An interesting side light on the corpus luteum is the belief of Finch[7] that women may vomit in early pregnancy because they are allergic to their own corpora lutea. He skin-tested women with hyperemesis and obtained positive reactions with commercial preparation of progesterone; negative reactions were obtained in patients who did not vomit. He also secured, in time, relief in certain cases where he produced desensitization. So far no corroboratory reports have appeared. It should be remembered also, from the purely scientific point of view, that modern commercial preparations of progesterone are synthetic, and that none of them are made from the human corpus luteum.

Based upon the supposition that estrin is secreted in small quantities in early pregnancy and then increases gradually to term, when enormous amounts are put out, Hawkinson[8] has suggested that pernicious vomiting may be caused by a deficiency of this hormone. He gave estrin to his patients, also with good success. He presents, however, no evidence to prove that less estrin than normal is secreted in pernicious vomiting. Moreover, recent work by Marrian, Cohen, and Watson[9] and by others has shown that estradiol, the active principle of estrin, is broken down in the body into two substances, estriol, and estrone, which is the more potent. Both exist in two forms—the so-called "free" form, and a form conjugated with glycuronic acid. Up to eight and a half months the "free" forms of both substances constitute only about 1 per cent of the total; after that they increase rapidly and may be the most important factor in bringing on labor. The usual animal assay methods, which do not reveal the presence of the conjugated estrogens, give values, therefore, that are actually far below the real amounts.

Little attention in this connection has been paid to the gonadotropic substance of pregnancy, which is secreted by the chorion in large quantities in the first month of pregnancy and gradually falls as gestation proceeds. It is the presence of this substance, of course, upon which the Aschheim-Zondek test depends. About the only writer who has used gonadotropic substance therapeutically is Fischer[10] who reported prompt relief after giving his patients, without their knowledge, retention enemata of their own urine. One wonders if the results would have been equally good if he had told them what he was doing.

Not only have the sex hormones been theoretically implicated in pernicious vomiting, but at least two other endocrines as well. Thirty-one years ago Rebaudi[11] suggested that the suprarenal glands might be at fault and in 1932 Kemp[12] expressed the opinion that these organs normally hypertrophy in pregnancy and may not do so in pernicious vomiting. In 1937 Freeman and Melick[13] reported forty-seven cases treated with cortical extract, accompanied, as one might expect, again by a favorable outcome. In the same year Sussman[14] reported good results in ambulatory patients after administering calcium and parathyroid extract.

When, as we have just seen, we have five different groups of observers curing pernicious vomiting with five different hormones, it is not surprising if we wonder just where the truth lies. Most mild cases of hyperemesis are readily relieved by simple measures. There is scarcely a condition in medicine that requires so much assurance on the part of the doctor and so much faith on the part of the patient. On the other hand the woman whose illness has defied the efforts of one or more physicians, and who at least enters the hospital firmly convinced that she will not be well until she is aborted, presents a problem that cannot be solved by hormonal shots in the dark—at least not in our experience.

Women with excessive vomiting are starved in proteins, carbohydrates, fats, minerals and vitamins. The most serious vitamin deficiency that develops is that of B complex which in some instances results in a polyneuritis differing in no way from that found in beriberi. Bleeding, spongy gums, and other signs suggestive of scurvy, or vitamin C deficiency, such as hematuria and periostitis, may appear. Retinal hemorrhages also have been reported.

Harding and Watson,[15] Titus and Dobbs[16] and

others have maintained that glycogen depletion in the liver is closely associated with pernicious vomiting. Glycogen depletion of the liver is not susceptible to proof even at autopsy, because immediately after death this substance is immediately converted to glucose. However, there is a certain amount of clinical evidence that indicates hepatic impairment, since in almost 80 per cent of our cases in which the icteric index was determined it was found above the normal. Also, in some severe cases, jaundice and bile in the urine are noted. We know that depletion of the hepatic glycogen store is produced by starvation, hence this phenomenon is much more likely to be the result of vomiting than its cause. Finally, therefore, we are forced to admit that no present theory concerning the pathogenesis of pernicious vomiting has been established to our complete satisfaction. It is possible that when the question is finally settled its solution may come through the refinements in chemical analysis which are now for the first time being applied to the sex hormones.

SYMPTOMS

The vomiting of hyperemesis gravidarum may vary from the simple ejection of recently ingested food to a constant reflux of the gastric contents. After the stomach has been emptied of food, the patient vomits first clear fluid, then bile-stained liquid of the characteristic thin pea soup character, and eventually an admixture of new or old blood, the latter producing the so-called coffee ground vomitus. The entrance of someone into the room, the slamming of a door, the raising of a window shade may be all that is necessary to precipitate an attack. Unless the patient's condition is most serious, the vomiting is diurnal and she is likely to sleep uninterruptedly at night. Because of starvation there is loss of weight, which is often marked and may be excessive. In advanced cases the skin is so loose that it may be picked up in folds. Dehydration results both from the inability of the individual to retain liquids and from the actual loss of fluid by vomiting. The skin is dry and rough, the tongue coated, the lips parched and cracked and may be covered with sores. The face is anxious, the eyes sunken, the general picture is one of marked misery and deep prostration.

The pulse rate in hyperemesis gravidarum is of great clinical importance. In our cases the highest rate recorded on the bi-daily chart was 100 or over in 89.9 per cent and 110 or over in 55.1 per cent. Among the patients that died the highest rate on the bi-daily chart was 110 in one case, 116 in one, 120 in two, 140 in one and 170 in one. F. S. Newell, former chief of staff of the Boston Lying-in Hospital, taught that a sustained pulse rate of 110 or over always indicated a very sick patient, and further experience has justified this belief.

The urine specimens of all patients on admission, were examined for acetone, diacetic acid, albumen and sugar. The icteric index was determined in sixty cases, the non-protein nitrogen in 154, the urea nitrogen in 137, the uric acid in 138. The CO_2 combining power was investigated in sixty-three cases. No attempt was made to ascertain the fasting blood sugar level on admission, since we considered it of prime importance to begin treatment at once. Hence we are unable to agree or disagree with Titus and with Harding, who believe that a hypoglycemia exists, or with Peckham[17] and with Dieckmann and Crossen,[18] who deny the existence of any such phenomenon.

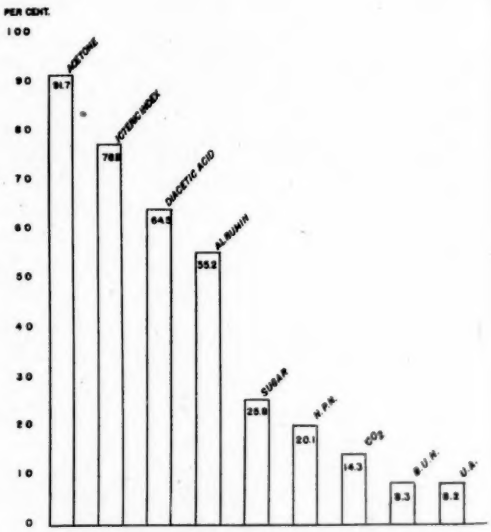

Fig. 3.—Results of laboratory studies.

In Figure 3 are shown the results of our laboratory investigations. The presence of a ketosis is almost the rule, which is not surprising, since most normal pregnant women will react in such a manner after a very short period of starvation. The presence of a high icteric index is significant and suggests involvement of the liver. In only a few cases was the CO_2 combining power below the normal for preg-

nancy, which shows that acidosis is not common in this condition. With the concentration of the blood that accompanies dehydration, an apparent increase in the non-protein nitrogenous constituents of the blood may be expected. Usually these values soon fall to normal after the patients receive sufficient fluid.

PROGNOSIS

As regards the outcome, we are concerned most with the maternal mortality and next with the necessity for therapeutic abortion. Fitzgerald and Webster,[19] in a study of 396 cases, reported fifteen deaths and thirty-two artificial terminations of pregnancy—incidences of 3.8 per cent and 8.1 per cent; and Naujoks,[20] in eighty-two cases, had two deaths, or 2.4 per cent, and twelve therapeutic abortions, or 14.7 per cent. The Report on Maternal Morbidity and Mortality in Scotland,[21] published in 1935, indicates that since 1911 about one in thirty of all deaths associated with pregnancy and childbirth were due to this cause.

Peripheral neuritis is, of course, the most serious complication of pernicious vomiting. In our series it occurred four times, or once in every fifty-six cases of hyperemesis, and one of these patients died. The clinical history shows that in practically every case the vomiting has persisted for a long time. It then ceases and the patient may begin to eat, but the pulse rate remains elevated. This is an important sign. Soon she begins to complain of muscular pains and weakness, usually beginning in the legs. The tendon reflexes are diminished or absent; wasting of the extremities, extensor paralyses, loss of sphincter control and nystagmus may follow. When peripheral neuritis occurs, the physician should always ask the patient if she has attempted to end her pregnancy by taking medicines, since some abortifacients containing apiol sometimes produce these symptoms by the presence of triorthocresyl phosphate. Immediate therapeutic abortion in peripheral neuritis often results in death; on the other hand if pregnancy is allowed to continue, even under massive feeding of vitamin B complex therapy, we have seen no marked improvement, and even prolonged invalidism. We believe that the ideal treatment is to terminate pregnancy if there is no improvement after about two weeks of intensive feeding, both by tube and by mouth, of a diet high in carbohydrate, protein and vitamins, fortified by large parenteral doses of thiamin chloride, ascorbic acid and liver extract.

Other chief complications in our series were puerperal psychosis and pyelitis, both of which occurred four times. Pulmonary tuberculosis was found twice, and hydatiform mole, renal tuberculosis, and acute appendicitis once each.

TREATMENT

The mild cases of vomiting which do not require admission to the hospital need no special comment. Reassurance, a fat free diet rich in carbohydrates taken in small amounts six or seven times a day, with a mild sedative, such as sodium luminal in half grain doses administered two or three times daily, will usually suffice. It is in this type of case that intramuscular injections of hormones evoke their most brilliant results; the physician may select what he believes to be the least illogical endocrine and give it to his patients, always provided he does it in a bold and convincing manner.

Such simple measures, however, are not enough for the patient who has been given up by her doctor and who is seriously sick. She can be treated successfully only in a hospital under complete isolation from her friends and family, including her husband. She is put to bed in a quiet darkened single room without the services of a special nurse. No emesis basin is left by the bed. The lower bowel is emptied by enemata and from three to nine grains of pentobarbital, or any suitable barbiturate, is given by rectum and repeated often enough to maintain the patient in a somnolent condition. Opiates are avoided as they appear to increase the vomiting. An initial hypodermoclysis of 1500 cc. of normal saline is followed by sufficient daily amounts to help maintain the fluid balance. An intravenous drip of 5 or 10 per cent glucose is given at the rate of thirty to forty drops a minute, and is repeated at intervals of from eight to twelve hours. In this way she receives 1000 to 1500 cc. of glucose solution in a day, and the total parenteral fluid intake is raised to at least 3000 cc. in twenty-four hours.

This method of treatment so far differs in no way from that in use in most maternity clinics. From January 1, 1928 to January 1, 1934 we treated in this manner 110 cases. Six patients, or 5.5 per cent died, and nineteen, or 17.3 per cent were subjected to therapeutic abortion. Considering the type of patient with which we had to deal the results were neither better nor worse than those reported from

other hospitals. Since the pathological changes in the patients who died were those of starvation, Teel[22] of our clinic then suggested that we use the Levine nasal tube as a method of forced feeding until the patient was able to take nourishment freely by mouth. After we had made this addition to our treatment at the beginning of 1934 the improvement was at once apparent. Up to January 1, 1940, we have treated 115 cases in this way with no deaths and with only three therapeutic abortions, a frequency of 2.6 per cent. The severity of the disease did not vary in the two series; in the first group 53.9 per cent had vomited for over a month before admission and in the second series 54.6 had vomited for an equal period. The results have been striking. Under our present regime the patient is isolated and receives sedatives, hypodermoclysis of salt solution and intravenous infusions of glucose solution as already described. In addition the Levine tube is passed and feeding carried out according to the following routine:

RESULTS

	1st Series, 1928-33, Parenteral Fluids, Sedatives	2nd Series, 1934-39 Levine Tube, Vitamin B High Carbohydrates
Cases	110	115
Therapeutic Abortion	19 (17.3 P.C.)	3 (2.6 P.C.)
Died	6 (5.5 P.C.)	0
Successful Cases	85 (77.2 P.C.)	112 (97.4 P.C.)

TABLE 1.

HOURS	
0	Levine tube passed and stomach gently washed with a small amount of warm water.
½	Murphy drip started. Four to 6 oz. milk containting 2 heaping teaspoonsful Harris' Yeast concentrate.
1½	Four to 6 oz. orange juice sweetened with Karo corn syrup.
2½	Six oz. rich egg-nog made with cream and egg.
3½	Milk and Harris' Yeast concentrate as above.

Repeat routine until fourteen out of twenty-five hours are completed.

Each feeding requires about forty minutes and is given at body temperature.

While we prefer that the tube should enter the duodenum it is by no means essential and equally good results may be expected even when its end is in the stomach. At the same time thiamin chloride, ascorbic acid and liver extract are given intramuscularly.

In conclusion, a word should be said about the cases in which no treatment succeeds, for there will always be a few. If in spite of the measures described there is a steadily rising pulse which remains well above 110, or if there is intractable vomiting with jaundice, the interruption of pregnancy is demanded. If twenty-four hours may be devoted to the process the safest procedure is to pack firmly the cervix and vagina, and the next day, after sufficient dilatation has been secured, to remove the ovum with the placenta forceps and the dull curet. Tearing or divulsion of the cervix must be avoided since the hemorrhage and shock resulting therefrom in a weakened patient may prove fatal. If time presses, vaginal hysterotomy may be performed. As regards anesthesia, avertin, because of its effect upon the liver, is interdicted. It is well, if possible, to avoid inhalation anesthesia, particularly chloroform and ether, but if the obstetrician elects to use it, nitrous oxide and oxygen, with preliminary medication with morphine or a barbiturate, is reasonably safe. Sacral, or low spinal anesthesia, if skillfully given, are perhaps the best of all.

SUMMARY

1. This report covers 225 consecutive cases of pernicious vomiting.

2. In a large maternity clinic this complication occurs about once in 176 pregnancies.

3. It is relatively infrequent among women of a low economic status.

4. Spontaneous abortion rarely occurs.

5. The pathology is that of starvation.

6. Recent theories of pathogenesis are discussed, and none is found convincing.

7. Ketonuria is almost the rule and has no prognostic importance.

8. Acidosis is uncommon.

9. Subclinical icterus is frequent.

10. By supplying an adequate fluid intake and by combating starvation by the use of the nasal tube, which supplies a nutritious fluid diet, combined with large doses of the essential vitamins, the frequency of therapeutic abortion has been reduced from 17.3 per cent to 2.6 per cent and the death rate from 5.5 per cent to zero.

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DISCUSSION

DR. E. NEWTON DUPUY, Beckley, W. Va.: We are taught that vomiting of pregnancy may be divided into three groups. Of the first, the neurotic type, too much cannot be said; I heartily agree with Dr. Irving that the personality of the physician in charge has more to do with the cures than the drugs or methods utilized.

The second, the reflex type, is recorded as being infrequent. But in my experience this is not a small group.

The third, the toxemic type, is the most severe. Here are found those cases arising from focal infections, deranged sugar metabolism, and the endocrinopathies.

The attributed etiological factors, are myriad. We have had thrust at us protein anti-bodies, placental antigens, the corpus luteum, glycogen deficiency, hysteria, the endocrines, etc. It seems most logical to me, and it is my belief, that the gonadotropic substance secreted in excess during the early weeks of pregnancy is the causative factor.

The treatment of this condition seems to vary with the individual—both patient and physician. The patients resisting treatment should by all means be hospitalized. I agree with Dr. Irving in strict and absolute isolation. I pay particular attention to the findings of the ophthalmologist at his daily examination and, when the first retinal hemorrhage occurs, then I believe therapeutic abortion is demanded within the hour. It is important to treat the patient psychically; to clear up any foci of infection; to treat any cervical erosion or retroversion of the uterus; to correct any anemia; to give adequate amounts of calcium, never forgetting its sedative action; to increase the intake of the various vitamins, with special reference to the Vitamin B complex; to restore the chlorides of the blood stream; and, most important of all, to increase the fluids with the idea of diluting or flushing out the excessive amount of gonadotropic substances.

DR. C. J. ANDREWS, Norfolk: There can be no doubt that the nausea and vomiting of pregnancy is a very dangerous condition. We are grateful to Dr. Irving for bringing us the results of his studies and telling us something to do about it. His paper clearly indicates that we do not know the etiology of the nausea of pregnancy itself, or its mechanism. However, the picture which results from continuous vomiting is a fairly constant thing so far as symptomatology and pathology are concerned.

Dr. Irving's figures are almost revolutionary. He stated that in one group he had 17 per cent therapeutic abortions and 5 per cent deaths, and his treatment reduced this figure to something like 3 per cent therapeutic abortions and no deaths. I don't believe we will be able to improve upon that.

Highly important in Dr. Irving's treatment is the use of vitamins in the control of nutritional deficiencies. While obstetricians, as a rule, are slow to take advice and to adopt new methods of technique, I believe the men in Virginia and West Virginia will use the suggestions which Dr. Irving has given us.

Some time ago we had occasion to study the follow-up on patients whom we had treated for sterility. These women want to be pregnant and it is interesting to note that they do not get nausea of pregnancy. No matter what may cause nausea of pregnancy, it certainly comes from the nervous system. The best time to treat the nausea of pregnancy is before the patient gets it. The doctor can best do this the first day a patient comes to his office.

In the treatment of nausea of pregnancy with bromide, one dose does almost no good; you have to give it until the level is up to a certain point. If you get the bromide level up to much over a hundred the patient will commence to have trouble. We usually start with 30 grains every six hours for two days, then twice a day and once a day, and give frequent meals containing high vitamin content. We make them eat six times a day whether they want it or not, and generally in a week they are all right. Once in a while when bromide doesn't work, we use a little phenobarbital. We have not seen a case of severe nausea in seven years. Our clinic patients are mostly negroes and they don't have nausea anyway. The method is so generally used that we rarely have a serious case.

DR. FREDERICK C. IRVING, closing the discussion: I think both Dr. DuPuy and Dr. Andrews brought up points that are extremely interesting. The psychic side of pernicious vomiting should not be ignored. Several

XUM

years ago a colleague of mine called me to see a patient in one of the suburbs of Boston. "She's terrible. She just lies there in bed and vomits", he said. She was a very healthy, rosy-cheeked, Irish woman. The Irish make very good obstetrical patients; they are very sturdy and can stand almost anything. I examined her and said, "Mrs. O'Rourke, the trouble with you is that your womb is hanging too low. Attached to your womb are a lot of nerves. You know how after a storm telephone wires sag and how it interferes with communication. That's the reason you are vomiting, the wires are out of commission and they telegraph bad news to your stomach. What I am going to do is to cure it". I produced a large, soft blown-up rubber pessary and I showed her that and said, "I'm going to put this inside and that is going to hold the womb up which will take the strain off those nerves and you will be well". Two months later my colleague called me and said "I wish you would come out to see that woman". I said, "Why didn't you tell me she wasn't any better". "Oh," he said, "she's fine. She hasn't vomited since you saw her, but I can't get that thing out of her."

THE TREATMENT OF ACUTE DELIRIA.*

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New York, N. Y.

The Psychiatric Division of Bellevue Hospital admitted over 28,000 patients during the year 1939. These cases represented every conceivable type of mental disorder. Because general hospitals wish to rid themselves of patients who are noisy, troublesome, uncooperative, suicidal or possibly dangerous to others, there is a constant stream of patients from the hospitals of New York City to the Psychiatric Division. During the year, the General Hospital of Bellevue transferred over 800 patients to the Psychiatric Division. A large number of these cases coming from general hospitals are restless, confused, delirious patients suffering from organic conditions of various kinds. They are usually transferred because they are too noisy or too uncooperative to be kept in general hospitals. In addition, there were approximately 12,000 alcoholic patients admitted in all stages, from mild intoxication to delirium tremens and Korsakoff's psychosis. Approximately 6,000 of our admissions were treated in the psychiatric medical or surgical wards which compose about 200 of our 630 beds. This number does not include the more disturbed patients who could not be kept on these wards but who could only be cared for on the wards especially designed for our most excited and disturbed patients. It will be seen, therefore, that the material at the Psychiatric Division of Bellevue Hospital includes all types of physical disorders, complicated by alcohol or some psychiatric condition. To cite a few examples, may I say that during the year 1939 we treated nearly 1,000 skull fracture cases, mostly complicated by alcoholism, and that we cared for approximately 200 cases of pneumonia, 150 cases of pulmonary tuberculosis, 1,500 cases of cardio-vascular disease, and nearly 2,000 cases of alcoholic psychosis, including 200 cases of alcoholic encephalopathy.

From such an experience in the treatment of excited and delirious patients, there are certain general principles of treatment which seem of importance and which can be emphasized. Although the cardinal principle of all treatment is to determine the precise cause of the disorder and treat the cause, and although there are many different causes for the deliria, there are certain general principles of treatment which remain the same throughout. Neglecting, therefore, the different causal factors which may require specific treatments, since such specific treatment is familiar to all of us, I shall concentrate on the factors which are common to all of these conditions and which can, in general, be treated in the same fashion, irrespective of whether the delirium is due to a specific organism or to various toxins.

Nearly four years ago we decided to make a systematic study of these delirious, excited and uncooperative patients. We considered what methods of treatment were being used and the reasons for using them. We tried to understand what was going on in our patients, what happens to a patient who is excited and delirious. Then we tried to work out better methods of treatment based on specific studies made at Bellevue as well as any new reports of studies which were relevant to our problems.

I believe that I can make my presentation much

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more vivid and interesting to you if I adopt the historical method of presentation and describe our progress, step by step, in working out better methods of treatment.

We first considered the problem of restraint and drugs. Restraint is used very frequently in the treatment of delirious and excited patients. The explanation commonly given is that the patient will not remain quiet in bed, that he may injure himself falling from bed, that he will exhaust himself by walking about or become chilled with resultant respiratory infection, and that he may harm himself or others.

We must admit that the average home or general hospital is not designed to care for overactive delirious patients. The structural arrangements of the average general hospital are satisfactory for treating other conditions but are seldem adequate for the care of the overactive, delirious patient. Restless, confused patients may fall out of windows or down shafts or stairs; they may secure drugs or sharp instruments and may harm themselves or others; they may be so noisy as to trouble the other patients; they may refuse to stay in bed and rush about with little or no clothing on—a situation which may be upsetting and disturbing to the other patients in the hospital and make impossible the retention of such a patient. Psychiatric hospitals are designed to prevent certain of these disturbances from occurring. Dangerous drugs and sharp instruments are kept away from the patient; the windows are guarded, and stairways are so arranged that patients cannot get to them. Provisions for segregating noisy patients and the use of sound-proofing devices help to make such patients less disturbing to others.

When a physician is treating an acutely delirious patient in a general hospital or at home, he is very likely to drug the patient or to forcibly restrain him for some of the reasons which I have enumerated. When he becomes too noisy or too disturbed, he is commonly labeled a mental case and transferred to a psychiatric hospital. I should like to point out, however, that many patients with obvious mental disorders are kept in general hospitals and that usually only the noisy, troublesome, or dangerous person is transferred to the psychiatric hospital. Coma is a mental disorder, but since the patient is quiet, remains in bed, and causes no disturbance, he is usually kept on in a general hospital, particularly if the cause of the coma is known and treatment is possible. If, however, the comatose patient requires tube feeding and is incontinent, he is very likely to be labeled a mental case and transferred to a psychiatric hospital.

In my opinion, a large percentage of restraint is due to lack of an adequate force of nurses. Our problem in such cases is to secure more nurses, but unfortunately budget limitations in hospitals and the private resources of patients do not enable us to do so. Under such conditions we must choose restraint as the lesser of the two evils but clearly recognizing it as an evil and never allowing ourselves to be satisfied with such a compromise.

The effect of applying restraint is often exactly the opposite of what is desired. The natural impulse of anyone is to struggle against restraint and many patients will exhaust themselves more rapidly in restraint than if allowed to get up and wander about.

We concluded, therefore, that while restraint might be necessary in some cases, it was usually of no value or was actually harmful to the patient and that the use of restraint should be kept at a minimum. Even when used it should not be allowed to remain on for long periods of time. Nurses were required to loosen a patient's restraint at least every two hours, any accidents may occur to patients in restraint and there is always the tendency of nurses to pay less attention to patients in restraint.

We may consider next the use of drugs. Drugs are commonly used to quiet delirious patients and put them to sleep. It may be argued, and with justification in some cases, that any harmful effect of the drug is more than offset by the quieting effect it has on the patient. This is undoubtedly true in a number of cases where restful, quiet sleep may be very important to a patient who is simply wearing himself out. An example of this is found in cases of cardiac decompensation where a state of confusion with fear and apprehension is very common. Many of these patients cannot relax or rest and something must be done to help the heart which is inadequate at best and which is rapidly being overwhelmed by the additional strain placed upon it. As an example of the beneficial use of drugs I would mention the use of morphine in cases of cardiac delirium. One of the best measures for relieving the anxiety and mild confusion of such cases is to give from ¼ to ½ grain of morphine intravenously. Usually after such medication the patient will quiet down and

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sleep for several hours, thus receiving marked benefit both mentally and physically. As a rule, however, morphine is not the best drug for treating excited, disturbed or delirious patients. Morphine relieves pain. If the patient cannot sleep because of pain, anything that relieves the pain will allow him to go to sleep. Under such conditions morphine, of course, will produce the desired effect. It may often relieve certain feelings of anxiety and tension. It is not, however, a particularly good drug to use in the treatment of excitement. I would like to quote from one of the greatest authorities in Psychiatry—Eugene Bleuler: "Opium and opiates are not hypnotics, but indirectly—by removing fear and psychic pain—they have a calming and even hypnotic effect. In psychoses, however, they do not achieve by far what their effects on the healthy would lead one to expect. With the exception of a few cases, their use can be dispensed with, and because the danger of habituation is very great, especially with psychopaths, there is good reason to avoid them as much as possible. To give opiates to an excited patient to facilitate transfer to an institution is hardly of any use, yet it constantly occurs, nevertheless." It may be pointed out further that morphine raises intracranial pressure and often masks signs of an associated intracerebral or intra-abdominal injury. One should also mention the old saying that morphine not only puts the patient to sleep but also the physician.

Hyoscine is a drug of somewhat uncertain effect, and one is inclined to use it as little as possible. It is frequently given with morphine. While this combination does have certain values, there are other drugs which are usually better and safer to employ.

Bromides have little value in severe excitement or delirium, their action being too mild. Because of their cumulative effects they should seldom be used.

Barbiturates are rather widely employed at the present time and the number of different derivatives is too great to attempt the description of each one. Sodium amytal has an almost specific effect in certain types of mental disorders but for quieting disturbed patients it is doubtful whether any of the various derivatives have any greater value than veronal itself. Many of the barbiturates are cumulative in their action; hence, if used over any long period of time, there is danger of producing a drug delirium. Particularly where bromides or barbiturates are being used to quiet a disturbed patient and where the patient gradually grows more disturbed, should the question of a drug delirium always be considered. In such cases it may be desirable to omit all medication for 24 to 48 hours to see if the patient quiets down. It may be stated as a general principle that hypnotics should be kept at a minimum in all cases of mental disorder and particularly so in acute delirium. As a general proposition, too much rather than too little drugging occurs. It is unnecessary to point out that in any suspected case, the urine, or better still the blood, should be tested for bromides and barbiturates.

If a hypnotic is necessary, paraldehyde is probably the best and safest one that we have. Because of its vile taste and odor many patients object to taking it. However, alcoholics seem to enjoy it and one might almost say that a definite diagnosis of alcoholism can be made by offering the patient a drink of paraldehyde. If he takes it eagerly and seems to enjoy it, he is undoubtedly an alcoholic. Paraldehyde can be given not only by mouth but also intravenously and by rectum. It is probably the most widely used hypnotic in psychiatric hospitals but appears to be less generally used by the rest of the medical profession. In cases where patients have difficulty in retaining anything by mouth, paraldehyde should be given either rectally by adding it to a small amount of milk so that it will be less irritating, or it may be given intravenously.

Another excellent hypnotic which has fallen somewhat into disfavor is chloral hydrate. As much as 30 grains may be given as a single dose, and this may be repeated in one hour if necessary. Chloral hydrate is a milder drug than paraldehyde and probably will not be so satisfactory for quieting extreme cases. In rather milder cases, however, it may work very well.

I would also mention the quieting affect of enemas. The reason for this is not entirely clear but experience has shown us that many restless, disturbed patients become quieter when given enemas. It does not seem likely that removal of toxic material from the intestinal tract would have such immediate effect. It has been suggested that dilatation of the intestine has secondary effects on the autonomic nervous system.

Two other methods of treatment are generally used in psychiatric hospitals but are less well known in general medical circles. The first of these is the continuous bath. The water of the bath should be slightly below body temperature, usually 96 to 98

degrees Fahrenheit. The patient reclines on a hammock suspended in the water and may be kept in the tub quite long periods of time, even days in some cases. Many patients are greatly quieted by such treatment. It is also excellent both for the prevention and treatment of bed sores. Since the main weight of the patient is supported by the water there is little pressure on the dependent parts. Furthermore, the constantly flowing water washes out the infected sores and promotes healing. A moderate degree of fever is not a contraindication. Neither is menstruation or post-partum states.

The cold wet pack is often of great value. Sheets dipped in cold tap water are wrung out and wrapped around the patient. Blankets are then added outside the sheets. A hot water bottle is placed at the feet and an ice cap or cold cloths to the head. Typically, the patient feels chilly, followed by a rush of blood to the skin with a feeling of warmth and relaxation. Many times a patient will go to sleep. Usually a patient should not be kept in a pack for more than 2 or 3 hours. It may be used cautiously, even with a high fever, but such patients must be watched continuously for any signs of collapse.

One of the first problems confronting us was how to combat dehydration and the acidosis and undernutrition usually accompanying it. Modern medicine has emphasized the forcing of fluids and a high caloric diet. The practical application of these principles was most unsatisfactory. Patients would refuse all liquids and food but an overactive, febrile patient needs more liquids and food than the normal person. Attempts to give large amounts of fluids intravenously were seldom successful. The patient would often struggle sufficiently to withdraw the needle from the lumen of the vein. It was obvious that we could not get enough fluid by intravenous or subcutaneous method. Passing a stomach tube and force feeding was likewise unsatisfactory. Many patients would vomit if one tried to give as much as 1,000 c.c. at a feeding. The danger of an aspiration pneumonia (and abscess formation) or of an acute asphyxia forced us to limit the feedings. After a careful study of the problem we came to the following conclusions.

The problem of dehydration is closely bound up with the loss of salt. Conversely, any attempt at hydration must consider the relation of salt and fluid. The average individual loses about 1,500 c.c. of fluid daily through the urine. But there are three other sources of water loss. About 400 c.c. of water is excreted from the lungs. Another 700 c.c. of water is diffused through the skin without the sweat glands being brought into action. The feces carry 100 c.c. of water from the system. The amount of fluid lost through the sweat is very variable. Thirty-three degrees Centigrade is the critical temperature of the skin. Below it, sweating does not occur. Above it, the sweat glands start to work. A person doing clerical work in cool weather loses from 200 to 500 c.c. of water through sweat. On this basis, one must supply 3,000 c.c. of fluid daily to prevent fluid loss. But if a person is active or febrile, he eliminates still more fluid, particularly through sweat.

Closely related to the loss of fluid is the loss of salt. The kidney normally puts out 15 gm. of salt every 24 hours when there is little salt loss through the sweat glands. There is a reciprocal relation between kidney and sweat glands. If the patient is overactive and febrile, more salt is eliminated through the skin. The sweat glands are more permeable to salt at high temperatures so that the percentage of salt loss in the sweat increases.

As an extreme example may be cited the experiment of a normal man walking up a treadmill for three hours with an air temperature of 50 degrees to 55 degrees Centigrade. Roughly 4,000 c.c. of fluid and 18 grams of salt were lost in his sweat. Cramps developed in the leg muscles soon after the experiment ended. After exertion in a hot environment sufficient to produce heat cramps, it is estimated that the total volume of blood in the body may be reduced as much as ten per cent. Since the blood becomes more concentrated, an analysis of the blood may show an apparent increase of chlorides. It is our opinion that deprivation of water and salt occurs in the tissues before it does in the blood and that the blood will draw on the tissues for any substance necessary to preserve its normal constituency. From all this, it appears that ordinary studies of blood chemistry tell us little about salt loss from the body as a whole.

It has been shown that heat cramps can develop even if one drinks large amounts of water. However, in 1922 Moss and Haldane pointed out that miners in Scotland who salted their beer and ate salty foods did not develop heat cramps, but that others did. Also many other studies have shown that heat cramps can be both prevented and cured

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by giving salt. We have recognized for a long time the necessity of forcing fluids in such cases but have not realized adequately the need of giving salt as well as fluid. If the salts of the body are depleted as well as the fluids, giving fluid without salt results in further elimination of fluid because there is not the salt necessary to keep it in the body, or if it is retained in the body it may cause edema. The recognition of the first part of this statement has led some to advocate the restriction of fluids in certain conditions such as head injuries and delirium tremens, feeling that forcing fluids will result in edema of the brain, thus harming rather than benefiting the patient. If, however, salt is given with fluids the edema will not occur and a very beneficial effect will be obtained by forcing fluids. In attempting to force fluids one frequently finds patients who object to taking further fluids. The patients feel water-logged and have great difficulty in taking more fluid, and it becomes difficult to build up the fluid intake to the desired amount. If, however, salt is given as well, the patient develops a thirst and oftentimes will spontaneously request more fluids. In every well run saloon there are dishes of salty popcorn, pretzels and highly spiced foods. It is well known that many chronic beer drinkers add salt to their beer. The reason for this is that it keeps up the amount of salt in the body even when large amounts of salt are being eliminated through the urine. One should emphasize, therefore, that as a general principle we force fluids but we also give considerable amounts of sodium chloride and probably some salt of calcium such as calcium lactate. It is possible to make up a fluid which will have much the same mineral constituents as normal blood and thus supply the needs of the body. Not only does salt enable the individual to drink more fluids, prevent the development of edema, and replace the salt lost through elimination, but, if the kidneys are functioning in normal fashion, salt will restore the normal electrolyte pattern. If the body is in an acid condition, chlorides will be eliminated and the acidity of the body will be decreased. If the body is too alkaline, sodium will be eliminated and the alkalinity of the body decreased. The use of fluids and salt, therefore, will largely combat dehydration and acidosis. Some persons find salt unpleasant to take and in some cases salt seems to irritate the stomach and cause vomiting. If enteric coated pills are used, these difficulties are done way with.

With these ideas in mind we started the treatment of our most excited and delirious patients by giving salt and forcing fluids. A large number of these cases were of alcoholic deliria. Two capsules of sodium chloride, 1 gram each, were given every four hours during the first day. Orange juice with one tablespoonful of sucrose in each glass constituted the bulk of all fluid given patients. Since the brain utilizes only carbohydrates, and McQuarrie's studies on diabetic children showed that the use of salt enabled the patient to metabolize more carbohydrates, it was felt that we had justification for giving the patient large amounts of sugar and salt. Also, in cases of liver damage there is a deficiency in glycogen reserve and it is important, therefore, to give carbohydrates. Utilizing this method of treatment for a period of eight months as compared with a six months' period prior to its institution, we found a drop of mortality rate from 17.3 per cent during the period preceding treatment to a mortality rate of 8.1 per cent during the time we gave salt and forced fluids. We found that patients who vomited frequently could usually retain orange juice. We also found that even when patients refused to drink, if a little orange juice was spilled on their lips they would often take the rest of the orange juice. In some cases we found that as soon as the patient had been given salt he would voluntarily request water. We also noted that when a patient had received considerable amounts of salt and fluid he often quieted down without having to receive hypnotics. Taking a second group who were not alcoholic we found that over a period of six months without special treatment there were 22 cases who showed marked dehydration; of these eight died. None of these patients had had fever due to dehydration on admission. For a period of five months we gave a patient who developed dehydration one gram of sodium chloride every four hours, or, of the patient had to be tube fed, he was given one quart of physiological solution of sodium chloride. Of the 14 patients who showed signs of dehydration with fever, not a single one died and the average duration of fever was 1½ days as compared with a duration of 7 days in the control group. Our experience was that, wherever possible, it was better to give salt and fluids by mouth rather than by the parenteral route, as there was not the danger to the circulatory system in trying to give large amounts of fluid. Pulmonary edema is likely to occur from large amounts of intravenous saline,

especially if given at a rapid rate. We found that a number of patients who died with fever due to dehydration had been given continuous infusions of physiological solution of sodium chloride. We also tried out the use of hypertonic solution of sodium chloride, giving 300 c.c. of a 5 per cent solution intravenously. In many cases we found that this had a quieting effect on the patients and that they would ask for water before the completion of the infusion. It was also felt that the temporary dehydrating effect of hypertonic solutions on the brain might be valuable in cases of deliria.

Following our experience with the beneficial action of forcing fluids and giving considerable quantities of sodium chloride, we endeavored to study the metabolism of these patients more carefully. In our alcoholic deliria we felt that the patient often had not been eating adequately for a considerable period of time and that a condition of starvation with acidosis and inability to assimilate carbohydrates normally was present. We did glucose tolerance tests on a number of these patients at the time of admission and then at a later date when they were convalescent. It was found that on admission the patients showed a sugar tolerance curve resembling that of a diabetic patient and that a week or so later, when convalescent, the sugar tolerance was improved and essentially normal. It was felt that the diminished tolerance was due primarily to an undernourished state which existed at the time of admission. With many of our patients it was often felt that there was considerable liver damage and that the organism was unable to store up glycogen and utilize it for nutritional purposes, and that many of our patients, therefore, would not have a reservoir of glycogen to draw upon and were unable to assimilate and utilize carbohydrates as well as the normal individual. All of this suggested the use of insulin together with fairly large doses of glucose as a means of combating the undernourishment of the patient. We also discovered that when a patient who has a high alcoholic content to his blood is given glucose and insulin, the alcohol will be eliminated from the blood at about twice the normal rate. Further, there is considerable evidence that insulin has a quieting effect on excited patients. I might point out that Sakel developed his theory of insulin shock treatment for schizophrenia from just this very fact. He first used insulin in the treatment of drug addicts with the idea that it had a quieting effect because of its action on the autonomic nervous system. Later he tried disturbed psychotic patients and discovered that when certain cases accidently went into insulin shock or coma they appeared to be greatly benefited. We have found by experience that in disturbed patients insulin often has a specific quieting effect. For all of these reasons, therefore, we instituted the use of glucose and insulin. Where patients will take glucose by mouth, one may give from 50 to 100 grams of glucose, together with 10 to 25 units of insulin. This may be repeated two or three times daily.

Although vitamin deficiency may have been overemphasized and considerable exploitation of the public may have occurred, I believe that we must consider carefully the vitamin status of our delirious patients. I would point out that Vitamin A has a definite value in building up the capacities of the organism to resist infection. Vitamin B, particularly B_1 and nicotinic acid, has a definite effect on brain metabolism and its absence may cause mental disorders. In Vitamin C deficiency a delirium with scurvy may develop. It is, therefore, of particular importance that Vitamins A, B_1, nicotinic acid and C be given in large doses to our patients. Vitamin B_1 has a fairly specific reaction toward the polyneuritis which often develops in alcoholic and other organic deliria. It is perhaps worthwhile to remind you that Korsakoff's original description of this psychosis characterized by a loss of memory replaced by confabulation and by polyneuritis was given to a group of cases most of which were not alcoholic but represented various organic conditions such as infectious and toxic states following childbirth, pneumonia, typhoid fever and arteriosclerosis. We have become so accustomed to thinking of Korsakoff's psychosis as due to alcohol that it is important to emphasize the fact that it is primarily a vitamin deficiency condition. The polyneuritis associated with Korsakoff's psychosis clears up excellently in response to Vitamin B_1. While it is doubtful if B_1 deficiency is the sole cause of the delirious picture, it may be one of the factors producing it.

Nicotinic acid seems to have a specific effect on certain severe deliria. In a paper on acute nicotinic acid deficiency encephalopathy, we pointed out: "This syndrome may occur as the only manifestation of a deficiency disease or may occur in association

with pellegra, polyneuritis due to Vitamin B_1 deficiency, the oculo-motor disturbances of a central neuritis, or scurvy. The clinical picture of this encephalopathic syndrome is more or less well defined and is characterized by clouding of consciousness, cogwheel rigidities of the extremities, and uncontrollable grasping and sucking reflexes."

A case study of 150 cases showing this encephalopathic syndrome shows that without vitamins practically all of these patients died, the actual rate being 95.7 per cent in 47 subjects; when to the usual treatment of hydration, thiamin chloride (B_1) was added, the mortality rate was 100 per cent in 15 subjects. When, however, the entire Vitamin B complex plus hydration was given, the mortality rate in 81 cases dropped to 61.9 per cent. In contrast with this, 22 consecutive patients were given nicotinic acid and only 31.8 per cent died. It appears, therefore, that a number of the acute deliria, particularly those occurring in alcoholic patients are definitely related to vitamin deficiency and that proper use of vitamins will aid in restoring many more of these patients.

It should be emphasized that these vitamin deficiencies may be superimposed on any delirious condition and thus produce serious complications. Prevention is better than cure, hence a high vitamin diet should be given all delirious patients.

Having carried out the various studies which I have mentioned and having applied them to the treatment of our patients, we have now evolved a certain routine for the treatment of all acutely disturbed and toxic patients. I shall describe this treatment as applied to the alcoholic delirium. The general principles are the same for all other deliria, but there will be certain variations in the treatment depending upon the cause of the delirium.

This treatment is based on the idea that the patient is probably suffering from dehydration, loss of salts, acidosis, malnutrition, vitamin deficiency and often gastritis and liver damage. The patient is excited, delirious and uncooperative. In the acute condition with extreme excitement, sedation may be necessary. The patient is commonly placed in a camisole while being treated but the camisole is removed as quickly as possible. Paraldehyde is the sedative of choice. If gastritis is present, paraldehyde is administered either rectally, giving about 3 to 6 grams diluted in milk, or intravenously 15 minims. 300 to 500 c.c. of 5 per cent saline with 10 per cent glucose intravenously is administered and insulin is given subcutaneously, 1 unit of insulin for every 2 grams of glucose. This whole routine should be given in less than half an hour if possible. The patient will usually quiet down and go to sleep.

As the patient improves, or in patients who are more cooperative and less toxic, the patient is placed in a tub and preferably given an enema in the continuous tub, after which the water is turned on for the regular continuous bath at approximately 96 degrees Fahrenheit. If the patient will take food or medication by mouth, he is first given ½ ounce of colloidal aluminum hydroxide for the purpose of soothing the inflamed mucosa of the gastro-intestinal tract. This is repeated twice a day. Sodium lactate is also given by mouth so that the patient receives approximately 50 grains a day. Salt tablets are given by mouth 2 or 3 times a day so that the patient gets a total of 90 grains of salt daily. The 5 per cent saline with 10 per cent glucose is given intravenously if necessary but wherever possible it is given by mouth. If the patient will take fluids freely he is encouraged to take orange juice which is usually well borne on a disturbed stomach. Glucose may be added to the orange juice if desired and insulin given as previously noted.

Special attention is paid to forcing vitamins. The patient is given Vitamin A in large doses but care must be taken not to give it in a way to upset the stomach. Vitamin B_1 is given up as high as 100 mgs. a day. This may be given in a single dose intravenously or it may be added to food by mouth. Nicotinic acid is given in 100 mgm. doses by mouth 5 to 10 times daily. If necessary, it may be given intravenously. Vitamin C should be given, at least 50 mgs. 3 times a day. If the patient receives large amounts of orange juice, he will, of course, receive sufficient Vitamin C in that fashion. Remember, however, that orange juice on standing loses most of its Vitamin C, unless kept in a refrigerator in a tightly closed container.

If the patient will not eat and if his stomach is not so inflamed as to make gastric feeding undesirable, the patient may be placed in a camisole, a stomach tube passed intranasally and then kept in position for several hours. The Levine tube is probably preferable as it is of sufficiently small caliber that it will not produce vomiting and gag reflexes as

much as a larger tube. With the tube one can start out by giving 100 c.c. of a 10 per cent saline solution. This is followed in about 20 minutes by 200 to 300 c.c. of water. In another 20 to 30 minutes this may be repeated. The amount given at each feeding should be sufficiently small so as not to provoke vomiting or to unduly upset the stomach. Large amounts are likely to induce vomiting and there is the danger of regurgitation which may be followed by aspiration which may even cause death at once by asphyxiation or it may set up a pneumonia. After giving approximately 1,000 c.c. of water one may give nutritive feeding. Glucose is probably the most easily absorbed form of energy and one very desirable feeding is to give 300 c.c. of orange juice with 50 grams of glucose added to it. Twenty-five units of insulin should be given at this time. The Levine tube is then withdrawn and restraint removed. As the patient improves, still further tub therapy is continued if possible, and the patient is allowed to take a more liberal diet. Colloidal aluminum hydroxide may be continued as long as gastritis is present, in which case the diet must, of course, be bland and non-irritating. Salt is continued at the rate of 90 grains a day in salt capsules. This makes the patient very thirsty and he will usually ask for water and drink large amounts. Orange juice can be given very freely. Insulin is continued in small decreasing doses both for its benefit in quieting the patient and for its effective assistance in the utilization of carbohydrates. Large amounts of vitamins are continued as outlined previously.

If this general routine is carried out in the treatment of acutely disturbed, delirious and uncooperative patients, I am certain that the period of delirium will be markedly shortened and the recovery rate will be greatly increased. It is understood, of course, that specific treatment is to be given in all cases depending upon the cause of the delirium and that individual modifications must be made when necessary. It is not intended that this treatment should be carried out in an absolutely fixed fashion, since the essence of the treatment of all patients is to individualize.

Bellevue Hospital.

DISCUSSION

DR. JOSEPH R. BLALOCK, Marion, Va.: We have all enjoyed very much Dr. Bowman's paper and wish to thank him for bringing before us in so clear and comprehensive a manner these particular studies that have been carried out by himself and his co-workers at Bellevue.

In no other psychopathic hospital in the country is there a greater number and variety of such acute problems, where patients have had to be shifted from general hospitals because they were considered too disturbed to be kept. Dr. Bowman has pointed out that the immediate essential problem lies in caring for the physical condition of the patient, and that certain cardinal principles of treatment must be followed. Putting into practice such general principles has resulted at Bellevue in marked reductions in mortality in special large groups, particularly in delirium tremens and nicotinic acid deficiency encephalopathy.

Only certain cities are fortunate enough to possess psychopathic hospitals or centers to which such patients may be sent for observation and treatment. Unfortunately, in Virginia at least, the physician, when a medically ill patient becomes mentally disturbed, may have to be adjudged legally insane, and sent to a State hospital, too often with a brief sojourn in jail. The psychotic condition clears up in a few days and the patient has been pronounced legally insane.

There should be established psychiatric pavilions or wards in every city or center where such patients may be treated. Furthermore, there should be provided in general hospitals one or two specially equipped rooms, with bath, toilet facilities and special windows. There are now screen windows available which are entirely escape-proof and appear just like any other screened window. Into such a room a delirious pneumonic patient, one with a bromide delirium, post-operative panic states, and other psychiatric problems may be cared for with safety. The physical therapy department should contain a tub for continuous bath, and its personnel should be able to administer sedative wet sheet packs. Since nurses are more and more receiving training in psychiatric nursing, they will be more competent to carry out the necessary special nursing procedures.

Concerning the bromide deliria:

Routine blood bromide determinations have revealed high blood bromide levels in a surprisingly large number of new admissions to State hospitals. A physician from one State hospital recently told me that his hospital was receiving fewer and fewer such patients because the general medical men in that part of the State were becoming more aware of this possibility, and disliked the chagrin of having one of their patients admitted with such a diagnosis.

I find that physicians in practice almost never use paraldehyde. They are also averse to using amytal or sodium amytal. I am in full sympathy with all that has been said concerning sedative treatment and restraint. We at our hospital are especially inclined to use continuous tubs, sedative wet sheet packs and colonic irrigations, so far as practical, in place of drug sedation.

I can add little to and only commend what has been said concerning the schedule of treatment as now used

at Bellevue. The chronological development is of special interest for we have all been attempting to keep up to date with the recent developments in various fields. For example, in 1935 Harris, Poliak and myself reported the treatment of a severe case of pellagra and alcoholism with recovery. A high vitamine diet, concentrated liver extract, vitavose, crystalline ascorbic acid, dilute hydrochloric acid, iron ammonium citrate, yeast tablets, a transfusion, all contributed to treatment. Nicotinic acid in its present form was not yet available.

Similarly in the early 1930's when the first general paralytics were receiving electrically induced fever no provision was made for the salt intake made necessary by the profuse sweating. These patients tolerated treatment much better when we commenced giving them sips of diluted or normal saline.

Again I wish to thank Dr. Bowman for his fine and eminently practical contribution.

DR. ARCHER A. WILSON, Charleston, W. Va.: Except in rare instances, morphine should not be used in cases of head injuries or cases of increased intracranial tension of whatever cause, because it further increases tension and depressess respiration, which may be already embarassed by the lesion responsible for the mental state. In addition, in head injuries, particularly, morphine may mask the very important pupillary changes and the all-important state of consciousness of the patient. There is no more justification for using it here than in an acute abdomen before a satisfactory diagnosis has been established.

Because of the extensive self-medication with the bromides and barbiturates, many confused and delirious patients may be found to be suffering from an accumulation of these drugs. For this reason, these drugs should be used with care where the necessity for their use extends over a period of time or where large doses are required for the control of a restless and noisy patient. We have found paraldehyde and avertin very useful for this type patient and the least objectionable of the various drugs.

Because of the studies of Dr. Bowman and his coworkers and of other investigators, the "encephalopathic syndrome", consisting of the clinical picture of clouding of consciousness, cogwell rigidities of the extremities, and uncontrollable grasping and sucking reflexes is now thought to be due to nicotinic acid deficiency and the previously high mortality rate has been markedly reduced by the use of nicotinic acid given in 5 per cent dextrose in normal saline. The treatment of delirium tremens has likewise been put upon a rational basis by the administration of a high caloric diet rich in vitamin B, glucose, sodium chloride and fluids.

Every effort should be made to determine the use of the mental disturbance. Common causes are the various infections, toxins, the insanities, drugs, alcohol, deficiency disease, dehydration, arteriosclerosis, brain tumors or abscess. Search should be made for evidence of a previous and often trivial head injury because a resulting chronic subdural hematoma often presents itself as a disturbance in consciousness or personality. If a cause can be found, then its specific treatment should be applied. Where a cause cannot be found, certain general measures are indicated. These call for the correction of fluid and electrolyte imbalance, proper feeding with attention to vitamin needs and indicated care for the physical condition of the patient.

Dr. Bowman's paper appears to suggest that something by way of preventive psychiatry might be employed by the giving of proper attention to the fluid and salt balances in the various medical and surgical illnesses and injuries. Thus those cases of deliria associated with fever and dehydration will not so likely occur.

The onset of active delirium is often heralded by sleeplessness and nervous irritability, anxiety, muscle twitching or apparent apathy. It would appear, therefore, that the judicious use of sedatives at this time would save patients, as well as the physician treating them, much mental anguish and worry.

Our duty as physicians demands that we exert as much expertness in anticipating and preventing unnecessary psychic trauma as in plucking out an offending part.

A CLASSIFICATION OF COMMERCIAL PREPARATIONS OF SEX HORMONES. II.[1]

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In a previous paper[2] the writer presented a tabulation of the commercial preparations of sex hormones, accompanied by a brief discussion of their functions and uses. Since that time additional products have been introduced, methods of standardization modified, and certain conceptions regarding them have changed.

The chief purpose of this paper is to bring up to date the tables which appeared in the former one. A brief discussion is included, however, to aid in their clarification. The hormones here discussed are taken up in the following order: equine gonadotro-

1. From the School of Pharmacy, Medical College of Virginia, Richmond.

2. *Virginia Medical Monthly*, 66:194, 1939.

*Died October 29, 1940. For reprints address R. J. Main, Medical College of Virginia, Richmond.

pin, chorionic gonadotropin, anterior pituitary products, the estrogenic hormones, the corpus luteum hormone, and the androgenic hormone.

Equine gonadotropin, thought to be formed by the placenta, is obtained from the serum of pregnant mares. It is not excreted by the kidneys to any material extent, but remains in the blood. Apparently it is an efficient stimulator of ovaries and testes. Since its administration is said to produce ovulation in the human subject, it is recommended chiefly for the treatment of sterility and certain types of amenorrhea. Its commercial preparations are set forth in Table 1.

Chorionic gonadotropin is believed to be elaborated by the human placenta and is excreted in the urine of pregnant women. Although it is used for various menstrual disturbances, the Council on Pharmacy and Chemistry of the American Medical Association endorses it for the treatment of cryptorchidism only.

A distinct advance has been made recently in the standardization of this hormone in that it is now

TABLE 1.—EQUINE GONADOTROPIN
(Pregnant mares' serum hormone—P. M. S.)
The International Unit (I.U.) is defined as the specific gonadotropic activity of 0.25 mg. (250 gamma) of the international standard preparation (one gamma equals .001 mg.).

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY
Cutter	Gonadin	500 I.U. per cc.
Schering	Anteron	Dry powder, ampuls 1.5 cc., 400 I.U. each
Upjohn	Gonadogen	Sterile tablets of 10 or 20 Cartland-Nelson units each (200 or 400 I.U.)*

*Am. J. Physiol., 122:201, 1938.

TABLE 2.—CHORIONIC GONADOTROPIN
(The anterior pituitary-like hormone—prolan)
The International Unit (I.U.) is defined as the activity present in 0.1 mg. (100 gamma) of international standard chorionic gonadotropin.

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY
Ayerst, McKenna and Harrison	A.P.L.	10 cc. vials, 100 I.U. per cc. 5 cc. and 10 cc. vials, 500 I.U. per cc.
Cole Chemical Co.	Chorionic Gonadotropin	10 cc. vials, 100 I.U. per cc. 10 cc. vials, 500 I.U. per cc.
Endo Products	Entromone	10 cc. vials, 125 I.U. per cc. 50 cc. vials, 125 I.U. per cc. 10 cc. vials, 500 I.U. per cc.
Harrower	Apestrin	10 cc. vials, 100 I.U. per cc. 10 cc. vials, 500 I.U. per cc.
Parke, Davis	Antuitrin-S	10 cc. vials, 100 Rat U. (approx. 120 I.U.) per cc. 50 cc. vials, 100 Rat U. (approx. 120 I.U.) per cc. 10 cc. vials, 500 Rat U. (approx. 600 I.U.) per cc.
Roche-Organon	Pregnyl	Dry powder, ampuls 1 cc., 100 I.U. 1 cc., 500 I.U.
Schering	Pranturon	Dry powder, ampuls 1.5 cc., 150 I.U. each 1.5 cc., 750 I.U. each
Squibb	Follutein	5 cc. vials, 500 I.U. each 10 cc. vials, 1000 I.U. each 5 cc. vials, 5000 I.U. each
Winthrop	Korotrin (formerly Korotron and Antophysin)	Dry powder Ampuls, 100 I.U. each Ampuls, 500 I.U. each Vials, 1000 I.U. each Vials, 5000 I.U. each Tablets, 150 I.U. each

evaluated in terms of "International Units" (I. U.). Formerly, several methods of assay were employed, each of which expressed its results in "rat units". A lack of uniformity in the methods used made it possible for a commercial product declaring a large number of rat units to be actually weaker than one declaring a much smaller number. Commercial preparations of chorionic gonadotropin are listed in Table 2.

The anterior pituitary gland produces the gonadotropic hormone, the thyrotropic hormone, the growth hormone, the lactogenic hormone, the adrenotropic hormone, and others. Table 3 presents commercial preparations which are made by extracting some of the above-mentioned principles from the anterior pituitary gland. The products of this table may differ widely in composition due to differences in the methods of manufacture. They are not necessarily comparable on a "unit for unit" basis, as is shown by the many methods of assay given in the footnotes of Table 3. These preparations are recommended in the treatment of dwarfism, menstrual disorders, sexual under-development, etc.

TABLE 3.—ANTERIOR PITUITARY GLAND EXTRACTION PRODUCTS

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY
Armour	Gonadotropic Factor	10 cc. vials, 300 R.U. per cc. (1)
	Growth Complex	10 cc. vials, 100 Growth U. per cc. (2)
	Polyansyn	10 cc. vials, 25 Growth U. (Collip) per cc. Also contains adrenotropic, thyrotropic, lactogenic and gonadotropic factors.
	Adrenotropic Factor	10 cc. vials, 10 units (Collip) per cc. (3)
	Thyrotropic Factor	10 cc. vials, 5 units (Rowlands-Parkes) per cc. (4)
Ayerst, McKenna and Harrison	Gonadotropic Factor	5 cc. and 10 cc. vials, at least 300 R.U. (Collip) per cc. (1)
	Growth Complex	5 cc. and 10 cc. vials. 1 cc. contains 100 Collip R.U. growth factor, 10 Collip R.U. adrenotropic and lactogenic factors. (2)
	Polyansyn	5 cc. and 10 cc. vials. 1 cc. represents 500 mg. of fresh bovine gland. Contains growth, adrenotropic, thyrotropic, lactogenic and a little gonadotropic factors.
	Prolactin	10 cc. vials, 100 units (Riddle and Bates) lactogenic hormone per cc.
	Thyrotrophic Factor	5 cc. vials, 50 R.U. (Collip) per cc.
Chappel	Prephysin	5 cc. and 15 cc. vials, 25 Fevold-Hisaw units (about 300 Collip clinical units) per cc. (5)
	Prephysin-Special-Potency	5 cc. vials, 100 Fevold-Hisaw (1000 Collip) units per cc.
Harrower	Anterior Pituitary Solution	10 cc. vials. Each cc. represents the soluble substance from 18½ gr. of fresh anterior lobe.
Parke, Davis	Antuitrin-Growth	20 cc. vials, 10 R.U. growth hormone per cc. (6)
Roche-Organon	Ambinon	1 cc. ampuls. Each represents 50 R.U. pituitary gonadotropic hormone and 200 guinea pig units thyrotropic hormone. (7)
Searle	Gynantrin	5 cc. and 15 cc. vials, 100 R.U. gonadotropic factor per cc. (8)
Squibb	Anterior Pituitary-Extract	20 cc. vials, containing 200 growth units, also thyrotropic and gonadotropic factors. (9)
Wilson Laboratories	Phyone	10 cc. and 30 cc. vials. 1 cc. is derived from 0.8 grams of fresh anterior tissue.
Italian Drugs Importing Co.	Prepituitary G	(Information not available.)

(1) One unit is one-tenth of that amount which, when administered daily in three divided doses for three days to a group of at least ten twenty-one-day-old female rats, each weighing between thirty and forty grams, produces ovaries having a combined weight of thirty-five milligrams, seventy-two hours after the first injection.

(2) Growth Factor: One unit is that amount which, when administered daily in two divided doses over a period of ten to fifteen days, by intraperitoneal injection into recently hypophysectomized but otherwise untreated rats weighing eighty to 120 grams, causes an increase in body weight of one gram per day.

(3) One unit is that amount which, when given daily in two divided doses to hypophysectomized rats for a period of one week, will give an increase of approximately 50 per cent in weight of the suprarenal glands as compared with those of untreated control animals. Animals are used for this test two weeks after the removal of the pituitary.

(4) One unit is the minimum quantity which, when administered daily in two divided doses for five days, will produce by the sixth day, definite hyperplasia and increase in the thyroid weight of the normal guinea pig weighing 200 Gms.

(5) One unit is that amount which, dissolved in 1½ cc. of liquid and injected in six injections (¼ cc. per injection) over a period of three days into immature rats (twenty-one days old) brings about an increase in the weight of the ovaries from 50 per cent to 100 per cent, as found in autopsy at the end of the fourth day. It is to be noted that this unit represents a potency equivalent to about ten to twelve Collip clinical units.

(6) A rat unit of Antuitrin-Growth is defined as the minimal daily amount which, when injected intraperitoneally into a mature female rat, will cause an average daily increase of 1 per cent in body weight over a period of at least ten days.

(7) One rat unit is the smallest amount of pituitary extract which, when combined with five rat units of Pregnyl, increases the average ovarian weight to 20 mg. in the test animals.

(8) Immature female white rats, weighing 35 to 45 grams, are given six equal subcutaneous injections over a period of three days, commencing when the rats are about twenty-six days old. The animals are autopsied 100 hours after the first injection. The ovaries and uteri are examined, removed and weighed after first expressing the fluid from the uterine cavity. Groups of at least six rats are used at each dose level. A "Rat Unit" is defined at the total dose required for each rat to produce an average increase of 50 per cent in uterine weight over that of controls. Corpora lutea are usually found at slightly higher dosage levels and are invariably present at the ten rat unit level.

(9) One growth unit is the minimal daily amount which, when injected each day for ten consecutive days into female rats (weighing 250 grams± 25 grams) will cause an increase of 10 per cent in body weight within an eleven-day period.

The ovaries secrete two well known hormones; (1) the estrogenic hormone, and (2) progesterone, the corpus luteum hormone. The title "estrogenic hormone", or "estrogen", is the general term for estradiol, estrone (theelin), estriol (theelol) and others. It is not definitely known whether estradiol or estrone is the secretory product of the ovaries. One may be secreted and later partially converted into the other in the follicular fluid, or both substances may be secreted simultaneously. They have the same therapeutic effect but differ in either intensity or duration. The benzoate and propionate of estradiol have a more prolonged effect on animals than do free estradiol or estrone. Estradiol and its esters are usually synthesized from estrone and estriol obtained from natural sources, such as pregnant mare urine. Estriol, the least potent of the three, gram for gram, is particularly adapted to oral administration because of its water solubility. The estrogenic hormone is recommended for the treatment of menopausal symptoms, gonorrheal vaginitis in children, senile vaginitis, menstrual disorders, infantilism and sterility. Its commercial preparations are set forth in Table 4.

TABLE 4—THE ESTROGENIC HORMONES

The International Unit (I.U.) of estrone is one ten-thousandth mg. (0.1 gamma, or 0.1 microgram) of a standard preparation of this chemical. The International Benzoate Unit (I.B.U.) is one ten-thousandth mg. of estradiol benzoate.

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY	TABLETS OR CAPSULES EACH:	VAGINAL SUPPOSITORIES EACH:	OINTMENT
Abbott	Estrone*	in oil: 1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 0.5 mg. 1 cc., 1.0 mg.		0.02 mg. 0.2 mg.	
	Estriol*		Capsules: 0.06 mg. 0.12 mg. 0.24 mg.		
Armour	Folestrin	in oil: 1 cc. 2,000 I.U. 1 cc. 5,000 I.U. 1 cc. 10,000 I.U. 1 cc. 20,000 I.U.	Capsules: 1,000 I.U. 2,000 I.U. 4,000 I.U.		
Ayerst, McKenna and Harrison	Emmenin	4 oz. bottles for oral use, 30 day-oral units (Collip) per cc.	Tablets: 120 day-oral units (Collip)		

TABLE 4—CONTINUED

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY	TABLETS OR CAPSULES EACH:	VAGINAL SUPPOSITORIES EACH:	OINTMENT
Ciba	Ovocylin (alpha estradiol)		Tablets 0.1 mg. 0.2 mg. 0.5 mg.	0.04 mg. 0.40 mg.	50 gm. tubes containing 0.03 or 0.15 mg. per gm.
	Ben-Ovocylin (alpha estradiol benzoate)	in oil: 1 cc., 0.083 mg. 1 cc., 0.1 mg. 1 cc., 0.166 mg. 1 cc., 0.2 mg. 1 cc., 0.333 mg. 1 cc., 1.0 mg. 1 cc., 1.66 mg.			
	Di-Ovocylin (alpha estradiol dipropionate)	in oil: 1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 1.0 mg. 1 cc., 2.5 mg. 1 cc., 5.0 mg.			
Cole Chemical Company	Estrogenic Hormone	in oil: 1 cc., 2,000 I.U. 1 cc., 5,000 I.U. 1 cc., 10,000 I.U.			
Endo Products	Estromone	in oil: 1 cc., 2,000 I.U. 1 cc., 5,000 I.U. 1 cc., 10,000 I.U. 1 cc., 20,000 I.U. 1 cc., 50,000 I.U.	Tablets: 1,000 I.U. 2,000 I.U. 4,000 I.U.		
Harrower	Plestrin	in oil: 1 cc. or 10 cc., each containing 2,000, 5,000 or 10,000 I.U. per cc.			
	Plestrin Topical	25 cc. dropper bottle, 2,000 I.U. per cc.			
	Plestrin Oral		Capsules: 1,000 I.U. 2,000 I.U.		
Lilly	Estrone*	in oil: 1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 0.5 mg. 1 cc., 1.0 mg.		0.2 mg.	
	Estriol*		Capsules: 0.06 mg. 0.12 mg. 0.24 mg.		
Parke, Davis	Theelin* (estrone)	in oil: 1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 0.5 mg. 1 cc., 1.0 mg.		0.2 mg.	
	Theelol* (estriol)		Capsules: 0.06 mg. 0.12 mg. 0.24 mg.		
Reed and Carnrick	Estrogenic Hormones	in oil: 1 cc., 5 cc., 10 cc., or 20 cc., each containing either 2,000 I.U., 6,000 I.U., 10,000 I.U., or 25,000 I.U. per cc.	Tablets: 1,000 .I.U		
Roche-Organon	Menformon ("natural estrogen")	in oil: 5 cc., 2,000 I.U. per cc. 5 cc., 10,000 I.U. per cc.	Tablets: 1,000 I.U. 10,000 I.U.	500 I.U. 1,000 I.U.	1 Gm. "dosules" containing: 2,000 I.U. or 5,000 I.U. each

TABLE 4—CONTINUED

MANUFACTURER	PROPRIETARY NAME	AMPUL OR VIAL SIZE AND POTENCY	TABLETS OR CAPSULES EACH:	VAGINAL SUPPOSITORIES EACH:	OINTMENT
Roche-Organon	Dimenformon (estradiol)		Tablets: 0.1 mg. 0.2 mg.		
	Dimenformon Benzoate (estradiol benzoate)	1 cc., 0.1 mg. 1 cc., 1/6 mg. 1 cc., 1/3 mg. 1 cc., 1.0 mg. 1 cc., 1-4/5 mg.			
	Dimenformon Dipropionate (estradiol dipropionate)	1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 1.0 mg. 1 cc., 2.5 mg. 1 cc., 5.0 mg.			
Schering	Progynon-B (estradiol benzoate)	in oil: 1 cc., 0.083 mg. 1 cc., 0.167 mg. 1 cc., 0.333 mg. 1 cc., 1.000 mg. 1 cc., 1.667 mg.			
	Progynon-DH (alpha estradiol)	in alcohol: 10 cc. vials for oral use. 0.3 mg. per cc. in oil: 30 cc. nebulizer containers for nasal spray, 160 R.U. per cc.	Tablets: 0.1 mg. 0.2 mg. 0.5 mg.	480 R.U. 4,800 R.U.	50 gm. jars 360 R.U. per gm. or 1,800 R.U. per gm. 25 gm. tube 1,800 R.U. per gm.
	Progynon-DP (estradiol dipropionate)	in oil: 1 cc., 0.1 mg. 1 cc., 0.2 mg. 1 cc., 1.0 mg. 1 cc., 2.5 mg. 1 cc., 5.0 mg.			
"One rat unit of Progynon-B or Progynon-DH is equivalent to approximately 10 I.U. of estrone."					
Schieffelin	Follacro (estradiol-17-propionate)	in oil: 1 cc., 1,000 R.U. 1 cc., 2,000 R.U. 1 cc., 5,000 R.U. 1 cc., 10,000 R.U.			
	Glovarian Pills		Pills: 500 I.U.		
Sharp and Dohme	Kestrone	in oil: 1 cc., 2,000 I.U. 1 cc., 5,000 I.U. 1 cc., 10,000 I.U.	Capsules: 1,000 I.U. 2,000 I.U. 4,000 I.U.		
Squibb	Amniotin*	in oil: 1 cc., 2,000 I.U. 1 cc., 5,000 I.U. 1 cc., 10,000 I.U. 1 cc., 20,000 I.U. for nasal administration: 5 cc. vial, 10,000 I.U. per cc. 30 cc. vial, 666 I.U. per cc.	Capsules: 1,000 I.U. 2,000 I.U. 4,000 I.U.	1,000 I.U. 2,000 I.U.	
Upjohn	Estrogenic Hormones	in oil: 1 cc., 2,000 I.U. 1 cc., 10,000 I.U.			
	Urestrin		Capsules: 1,000 I.U. 2,000 I.U.		

*Accepted by the Council on Pharmacy and Chemistry of the A.M.A.

TABLE 5—PROGESTERONE
(The corpus luteum hormone)
One International Unit (I.U.) represents one mg. of C. P. progesterone.

MANUFACTURER	MANUFACTURER'S NAME	1 CC. AMPULS EACH CONTAINING IN OIL:	TABLETS EACH:
Abbott	Progestin	1, 2 or 5 I.U.	
Armour	Progesterone	½, 1, 2 or 5 I.U.	
Ciba	Lutocylin	1, 5 or 10 I.U.	
Endo Products	Lutromone (formerly Lutrone)	1/5, ½, or 1 I.U.	
Harrower	Luteocrin ("natural progestin")	½ I.U.	
Lilly	Progestin	1, 2 or 5 I.U.	
Parke, Davis	Lipo-Lutin	1 or 2 I.U.	
Roche-Organon	Progestin	1, 5 or 10 mg.	
Schering	Proluton	½, 1, 2, 5 or 10 I.U.	
	Pranone (anhydrohydroxy-progesterone)		5 or 10 mg. "Orally effective in ratio 5 mg.=1 mg. Proluton"
Schieffelin	Progesterone	1, 2 or 5 I.U.	
Upjohn	Progesterone	1 I.U.	
	Progestin ("natural corpus luteum hormone")	½ or 1 Corner and Allen Rabbit unit.*	

*The Corner and Allen rabbit unit is the minimal quantity which, divided into five equal daily doses, produces on the sixth day a degree of progestational proliferation equal to that found in the uterus on the eighth day of a normal pregnancy.

TABLE 6—THE ANDROGENIC HORMONE
(The male sex hormone)

MANUFACTURER	PROPRIETARY NAME	1 CC. AMPULS EACH CONTAINING IN OIL:	OINTMENT
Ciba	Perandren (testosterone propionate)	5, 10 or 25 mg.	50 gram tubes containing 2 mg. testosterone propionate per mg. 2 gm. tubes "ointlets" same strength.
Endo Products	Virosterone ("from natural sources")	1, 3 or 5 capon units (1)	
Harrower	Lydin ("from bovine testes")	2 capon units (2)	
Roche-Organon	Neo-Hombreol (testosterone propionate)	5, 10 or 25 mg.	2 gm. "dosules" containing 4 mg. testosterone propionate.
Schering	Oreton (testosterone propionate)	5, 10 or 25 mg.	Oreton-F. 50 gm. tube and 2 gm. "Toplicator". Each contains 2 mg. free testosterone per gm.

(1) The capon unit is the amount of material required by injection over a period of five consecutive days to cause an increase of the capon comb (length plus height) of from three to seven millimeters by the sixth day, in at least five out of ten injected capons.

(2) One capon unit is the amount of solution which, injected into a leghorn capon daily for five days, will produce an average of 5 mm. increase in the length plus height of the comb.

The corpus luteum hormone, progesterone, is essential to the maintenance of pregnancy by its action on the uterine lining. It is now preparaed synthetically and is recommended in cases of menstrual disorders, threatened or habitual abortion, dysmenorrhea, sterility, etc. The estrogenic hormone stimulates uterine contractions, progesterone inhibits them. The commercial preparations of this hormone are listed in Table 5.

The male sex hormone, secreted by the testes, is known as testosterone. It undergoes a slight change in the body and is eliminated in the urine as androsterone. These two compounds have chemical formulae which closely resemble each other and those of estrone, estriol, estradiol and progesterone. Both testosterone and androsterone can be recovered from natural sources or made synthetically. Since testosterone is more active it is used clinically. The action of testosterone propionate is more prolonged than that of free testosterone. It is recommended in the treatment of infantilism, impotence, prostatic disorders, abnormal menstruation, and sterility. Its commercial preparations are presented in Table 6.

HEPATIC PHYSIOLOGY.*

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As the first speaker on this program, it apparently falls to my lot to define our subject, which I will do in the simplest way by saying that jaundice is the yellow staining of skin and conjunctiva due to the excessive retention of bile pigments in the body. This condition may be caused by (1) an abnormally rapid production of pigments, as in hemolytic jaundice, or (2) more usually by failure of excretion due to damage of the hepatic cells or blockage of bile drainage.

The dangerous symptoms of the icteric patient, however, are not due to these bile pigments, which are innocuous. Rather are they due to disturbances of liver function. For instance, the prolonged clotting time in hepatic icterus is apparently due to the interference with fat absorption, caused by lack of bile salts in the intestine. This results in a lack of absorption of vitamin K, which, in turn, causes a drop in the prothrombin content of the blood. It must not be forgotten, however, that other fat soluble vitamins will likewise not be absorbed normally, for it has been shown that pre-operative administration of vitamin D and Ca to patients with liver damage has a beneficial effect on bleeding time. Likewise, these patients may also suffer from an A avitaminosis.

Other symptoms of icterus, such as pruritis and bradycardia, may be due to the accumulation of the toxic bile salts in the blood, or to failure of the detoxication function of the liver.

*Read as part of a Symposium on Jaundice before the Medical Section of the Virginia Academy of Science, at Lexington, Va., May 3, 1940.

A. Since the bile pigments are responsible for the name of this disease, let us first consider their metabolism. Unfortunately there are several theories concerning certain details of this, so I will merely discuss one of them. Effete red blood cells are engulfed by the reticulo-endothelial cells, especially of the bone marrow, but also of spleen and liver. Here the hemoglobin is broken down through the following stages:

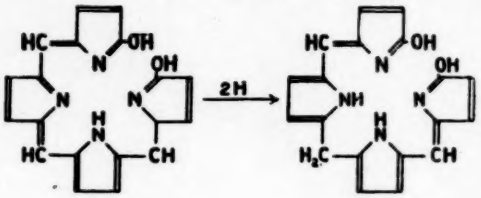
Hemoglobin ⇒ *Hemochromogen* ⇒ *Verdohemochromogen* (a green, Fe containing, protein pigment) ⇒ *Biliverdin* + Fe + globin. The Fe is stored in liver and spleen for further use, and the globin is probably metabolized like any protein. This green *Biliverdin* may pass into the blood as such, or most may be broken down into the yellowish-brown *Bilirubin*, which then passes into the blood.

These pigments pass to the liver, where they are removed by the hepatic cells and excreted in the bile into the gut. Here by bacterial reduction, part is changed to the brown *Stercobolin* of the feces, but most is reduced to yellow *Urobilin*, some of which may be excreted, but most of which is further reduced to colorless *Urobilinogen*, part of which may be excreted in the feces, and the rest reabsorbed into the blood. Part is then excreted in the urine, where, on standing, it is oxidized to yellow *Urobilin*. The major part, however, passes again through the hepatic cells, which oxidize most to *Bilirubin*, although some may remain unchanged, and both are excreted into the gut in the bile to renew the cycle. Thus human

bile contains *Bilirubin, Biliverdin,* and *Urobilinogen.*

If, however, due to hepatic damage or blockage of bile drainage, the liver cannot excrete these pigments, then the *Bilirubin* coming from the reticulo-endothelial system may be excreted in the urine.

The structural formulae of the two chief bile pigments are as follows, the others being very similar:



Biliverdin Bilirubin

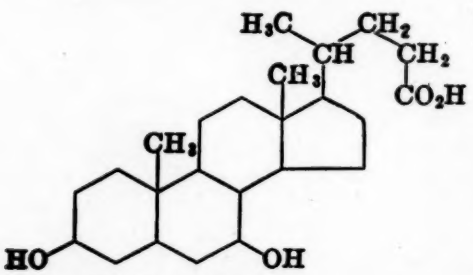
B. Since some of the symptoms of icterus may be due to the effects of retained bile salts, let us next discuss their metabolism.

The bile salts are actually synthesized by the liver, instead of being merely excreted, as are the bile pigments. The two salts present in largest quantities in human bile are Na glycocholate and Na taurocholate, with small amounts of Na cholate, choleate, and desoxycholate. The first two are Na salts of glycocholic and taurocholic acids. By hydrolysis, these two acids have been shown to be composed as follows:

$$C_{23}H_{36}(OH)_3CONHCH_2COOH \rightarrow C_{23}H_{36}(OH)_3COOH + CH_2(NH_2)COOH$$
(glycocholic acid) (cholic acid) (glycine, an amino acid)

$$C_{23}H_{36}(OH)_3CONHCH_2CH_2SO_3H \rightarrow \text{cholic acid} + CH_2(NH_2)CH_2SO_3H$$
(taurocholic acid) (taurine)

The structural formula of cholic acid is as follows:



Cholic acid

It will be noted that this is structurally very similar to the formulae of cholesterol, ergosterol, vitamin D, the androgenic and estrogenic hormones, progesterone, and corticosterone. Little is known of the mechanism of synthesis of these bile salts, except to suspect that cholesterol is their precursor. Although these salts are definitely toxic, and quite capable of producing such effects as hemolysis in vitro, and bradycardia, it is not known whether some of the icteric symptoms are due to bile salt retention or not.

The physiologic effect of bile salts in the intestine is extremely important. Due to their ability to lower surface tension, they probably assist in emulsification of lipoids, thus affording a greater area for attack by the lipase. They then assist in the absorption of these lipoids, apparently by uniting with them to form a more soluble compound—the hydrotropic effect. Thus a considerable part of the bile salts is reabsorbed, to be excreted by the liver in the bile, which saves the liver from having to manufacture as much as it would if no absorption occurred. As these salts are excreted by the liver, they apparently stimulate the formation of larger quantities of bile, thus exerting the important cholergic effect of bile salts. There is also some evidence that these chemicals increase the motility of the intestine. To digress slightly at this point, I wish to state my hope that the ancient superstition of calomel being a cholagogue has died a warranted death. It must be made clear that a choleretic is a substance which increases secretion of bile, such as bile salts and secretin, whereas a cholagogue is a substance which causes evacuation of the gall bladder, as cholecystokinin, or magnesium sulfate.

C. The bile may be described as follows:

Color: Brown-yellow (hepatic); orange-brown (cystic).

Amount: 500 to 1,000 cc. per twenty-four hours, depending on the type of diet.

pH: 8.6 (hepatic) to 5.7 (cystic).

Osmotic concentration: Isotonic (hepatic) to slightly more than isotonic (cystic).

Constituents:

H_2O (97 per cent).

Pigments: Bilirubin, biliverdin, urobilinogen.

Bile salts (5 gm./24 hrs.): Na glycocholate, Na taurocholate, Na cholate, choleate, desoxycholate.

Enzymes: None.

Minerals: Na, K, P, Ca, Mg, Fe, Cu, PO_4, SO_4, CO_3.

Protein: Phosphomucin.

Lipoids: Cholesterol (6 gm./24 hrs), lecithin.

Miscellaneous: Urea, indican.

Abnormal constituents: Drugs, metals, dyes, glucose, etc.

The functions of bile may be summarized as follows:

1. *Digestion*—
   Bile salts:
   a. Emulsify fats.
   b. Activation of pancreatic lipase.
   c. Hydrotropic absorption of fat, vitamins, Ca.
   d. Increased motility of gut.
   e. Choleretic.
   f. Solution of excreted cholesterol.
2. *Excretion*—
   a. Bile pigments and dyes.
   b. Metals (As, P, Fe, Cu, Ca, Zn).
   c. Cholesterol and lecithin.

Thus the chief functions of bile include the supply of bile salts for digestion, the buffering (even though acid in pH) of the acidic gastric contents entering the duodenum, and excretion of various substances.

D. The gall bladder: Alkaline hepatic bile is stored in the gall bladder, where it is concentrated by absorption through lymphatics or capillaries of water and certain constituents, so that the amount of basic minerals is about doubled, Ca is increased five times, Cl is diminished five times, $\overline{HCO_3}$ disappears, bile salts are concentrated about five times, and the pH becomes acid. The advantage of this process is apparently that there is now on hand a large amount of concentrated bile ready to deal with large quantities of fat that may be ingested.

The gall bladder may likewise act as a pressure valve, in that during a peristalic contraction of the duodenum, which closes the sphincter of Oddi, the hepatic bile under secretory pressure of the liver, instead of tending to distend the biliary ducts, can pass into the bladder. The lack of such a pressure valve may explain the distension of the larger bile ducts commonly following cholecystectomy.

The gall bladder musculature is stimulated to contract by the hormone cholecystokinin which is formed in the duodenum by certain fats, as egg yolk, olive oil, and cream. $MgSO_4$ causes evacuation of this organ, probably by causing relaxation of the sphincter. Consequently, when fasting or on a carbohydrate diet, the biliary flow is extremely small, as compared to a normal or high fat diet.

E. Finally, let us briefly renew the functions of the entire liver, since disturbances of some of these functions may be responsible for certain symptoms in jaundiced patients.

LIVER FUNCTIONS

1. Protein metabolism—
   a. deamination of amino acids
   b. urea formation
   c. synthesis of amino acids
   d. formation of prothrombin, fibrinogen, globulin? albumin?
2. Carbohydrate metabolism—
   a. glycogen formation and storage (galactose ⇒ glycogen test)
3. Fat metabolism—
   a. formation of ketones
   b. desaturation of fats
   c. excretion of cholesterol
4. Vitamins—
   carotene ⇒ vitamin A; storage of vitamins A, B complex, D, K
5. Storehouse—
   P. A. factor, Fe, Cu
6. Excretion—
   toxins, metals, bile pigments (dyes, radio-opaque substances)
7. Detoxication—
   indole ⇒ indican, etc. (benzoic acid ⇒ hippuric acid test)
8. Bile secretion and bile salt formation
9. Reticulo-endothelial system
10. Heparin formation
11. Blood volume and water concentration (heat regulation)
12. Bacterial filter for portal blood

Finally, may I digress once more to stress my hope that the fanfare attending clinicians thronging to climb on the band-wagon of the pre-operative use of vitamin K with bile salts, may not drown out the few voices asserting that lack of other fat soluble vitamins, as A and D, may also be of importance, even though their lack may not be so spectacularly, rapidly, and simply demonstrated as is a K avitaminosis. Moreover, a synthetic and water soluble vitamin K is now being used with excellent results, orally or intravenously, without the necessity of administration of bile salts.

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THE CLINICAL ASPECTS OF JAUNDICE.*

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As is indicated by the title of this discussion, we are concerned today with those aspects of jaundice that are of immediate practical importance to the clinician. The physician at the bedside observes the presence of jaundice and desires to interpret this phenomenon in terms of a definite pathological condition or conditions. His decision as to the course of treatment adopted in a particular case will be largely influenced by his understanding of the nature of the underlying process that is producing this symptom. It seems clear, however, that one cannot arrive at an accurate conception of jaundice clinically without at least a general understanding of the basic physiological and pathological factors concerned in the formation of bilirubin and its excretion by the liver.

As far as is now known there is one source and only one source of bilirubin; that is, the released hemoglobin of destroyed erythrocytes. The splitting of hemoglobin into an iron-containing fraction and bilirubin takes place principally in the bone marrow, and to a lesser extent in the spleen and the liver. It is believed that this process is carried on by the cells of the reticuloendothelial system. Extravasated blood undergoes hemolysis and conversion of blood pigment into bilirubin *in situ*. From these factories bilirubin is transported by the blood stream to the liver and if the liver is normal it is excreted by the liver cells into the bile ducts. This process proceeds continuously in the normal animal. There is a constant supply of senile erythrocytes that are continually being disposed of so that a steady supply of bile pigment is carried from these reservoirs by the blood stream to the liver and regularly delivered into the bile ducts. It is evident that the amount of bilirubin formed will be quantitatively affected by the supply of erythrocytes and by their rate of hemolysis.

It can not be shown that the liver has a definite threshold for bilirubin, such as the kidney has for sugar, but a more or less constant level of bilirubin is maintained in the blood similar to the normal level of certain metabolites that are excreted by the kidneys. Just as the kidney has a large reserve above ordinary demands, so is the liver able to sustain extensive damage and still preserve its function of excreting bile pigment. McMasters and Rous have shown that 95 per cent of the liver of a monkey or a dog may be destroyed and the function of excreting bilirubin still be maintained by the remaining 5 per cent. Under normal conditions bile pigment in the blood is extracted by the epithelial cells of the liver, excreted into the bile canaliculi, and thence finds its way into the intestines through the system of biliary ducts.

Jaundice exists whenever the normal limit of bile pigment is exceeded in the blood. Jaundice does not become visible in the skin and sclera until there is approximately a three-fold increase above the normal amount of serum bilirubin. There exists, therefore, a definite zone of invisible or latent jaundice. The presence of latent jaundice may be detected by determining the degree of yellow color in the serum (icterus index) or by estimating quantitatively the actual amount of serum bilirubin present.

From a consideration of these facts it is apparent that jaundice may arise in one of several ways, namely:

1. Over-production of bile pigment to the point that it can not be effectively removed by the normal liver.

2. Damage to the liver cells that will prevent normal absorption of bile pigment from the blood stream and its discharge into the bile ducts.

3. Obstruction of the bile ducts either by multiple involvement of the small ducts or by occlusion of the hepatic or the common duct.

4. By some combination of these.

The first condition set forth rarely occurs because of the great reserve power of the liver. An enormous amount of hemoglobin must suddenly be set free if jaundice is to result from this cause. It must be admitted that this is possible, however. A woman who had previously been well experienced a severe chill followed by a rise of temperature to 105°. Following this her color changed to a deep copper red and the urine became the color of a strong iodine solution. The blood serum was red from the presence of free hemoglobin. Within twenty-four hours the red color

*Read as part of a Symposium on Jaundice before the Medical Section of the Virginia Academy of Science, at Lexington, Va., May 3, 1940.

of the skin had disappeared, the patient was quite yellow, and the blood serum contained a large excess of serum bilirubin.

The second condition frequently exists, but in order to cause jaundice the degree of liver damage must be severe. It has been pointed out that in certain animals as little as 5 per cent of normally functioning liver tissue is sufficient to rid the blood stream of excess bile pigment.

The third possibility needs no comment except to emphasize the fact that in order to produce jaundice by obstruction the blockage must be either in the hepatic or the common duct, or the involvement of the smaller ducts must be general. Occlusion of a large branch of the hepatic duct will not produce jaundice.

The fourth possibility is the mechanism usually at work. If there is excessive hemolysis of red blood cells going on in the body, there will be an associated anemia. As a consequence of the resulting poor oxygen supply, the liver cells are damaged and are less capable of excreting the excess of bilirubin. In toxic liver injury, blockage of the bile canaliculi occurs with consequent regurgitation of bile into the blood stream. In gross obstruction of the hepatic or common duct, evidence of injury to the liver cells due to back pressure soon appears.

The old classification of jaundice into obstructive and non-obstructive jaundice is of little value since non-obstructive jaundice is purely a negative term and conveys no particular meaning. McNee's classification into hemolytic, toxic infectious, and obstructive, is helpful. In the hemolytic group are included all conditions associated with the over-production of bile pigment. The inference may be drawn that the factor of over-production alone is responsible for the jaundice, but this is not necessarily true. The toxic infectious group includes those cases of jaundice due to injury to the liver cells by chemical agents or bacterial toxins. The obstructive group corresponds to the obstructive type in the old classification.

The classification of Rich is more detailed and gives a clearer understanding of the underlying factors concerned in the production of jaundice, and from the clinical standpoint is as easy of interpretation. He divides all jaundice into two groups; retention jaundice and regurgitant jaundice. Retention jaundice comprises those cases with increased production of bilirubin. Rich believes, however, that over-production of pigment will not, as a rule, result in jaundice in the presence of a normal liver, but that for the occurrence of jaundice there must be a concomitant injury to the secretory cells of the liver. He believes this added factor to be an associated anemia that results in injury or even death of the epithelial cells of the liver. In the case of jaundice neonatorum the associated factor is immaturity of the liver cells with a resultant lowered secretory power.

Regurgitant jaundice is divided into two distinct types: that associated with injury of the liver cells and that due to obstruction of the bile ducts. The advantage of this classification lies in the circumstance that it affords a clear interpretation of certain clinical and laboratory observations on jaundice. An example is afforded by a consideration of the important differences between bilirubin as preformed in the blood and that present in the bile after passage through the liver cells. It is thought that as bile pigment enters the blood stream from the reticuloendothelial cells it is absorbed by or combined with some substance in the blood plasma. On its passage through the liver this combination is released. According to Eller, bilirubin exists in the blood plasma in a colloidal state and in the liver bile in a crystalloid form. Whatever the explanation, certain differences do exist. Plasma bilirubin has a lower color value, it is less easily excreted by the kidneys, and it is less readily oxidized. As a consequence of this, it does not react immediately with Erlich's diazo reagent but gives the so-called indirect type of reaction. Bile pigment that has been excreted by the liver cells and then returned to the blood stream will be excreted by the kidneys at a much lower level of concentration. It has a higher color value and will thus give a higher reading on the icterus index scale as compared with the same amount of retained bilirubin. This is the form of bilirubin that gives the immediate direct reaction with the diazo reagent.

Over-production of bile pigment and its retention due to secondary liver injury may occur as a result of numerous disease processes, such as pernicious anemia, hemolytic familial jaundice, hemolytic septicemia, and malaria. In the pure state of retention jaundice resulting from these diseases certain diagnostic features are to be noted. The blood serum gives an indirect Van den Bergh. The urine is free of bile but shows an increase of urobilinogen. There is an increased amount of urobilin in the feces and the spleen is usually enlarged. Anemia is nearly

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always present and often to a severe degree. In addition are to be noted the special diagnostic features of the several diseases that may produce this type of jaundice. As a rule, jaundice in a pure form does not long persist, but is rapidly modified by a secondary damage to the liver cells or by the development of obstruction in the small liver ducts. It is to be noted that about half of the cases of familial jaundice are complicated by the presence of gall stones. Since the conditions associated with retention jaundice have quite definite clinical pictures and since a correct diagnosis will readily follow clinical study, they will not be considered in detail.

The more important clinical problem revolves around a differentiation of obstructive jaundice and jaundice due to severe injury or necrosis of the liver cells. This differentiation, while of first importance, is not easy and at times is quite impossible. The importance of making such a decision lies in the fact that persistent obstruction of the bile duct will lead to secondary injury to the liver and it is thus desirable to relieve obstruction early. Furthermore, as the severity of the jaundice increases and as the injury to the liver progresses, the patient becomes an increasingly poor operative risk. On the other hand, operation on a case of toxic or infectious jaundice accomplishes nothing and adds greatly to the patient's handicap.

There is no single test or observation that we can rely upon to positively differentiate these conditions. Rather must we arrive at an opinion, more than a diagnosis, by joining together a number of facts and observations. A careful review of the history, certain points in the physical examination, studies of the urine, stool and duodenal contents, frequent observations on the quantity of bilirubin in the blood, determination of blood cholesterol and its partitions, and certain liver function studies, all may be necessary factors in forming an opinion as to the cause of jaundice in a given case.

The reason for the difficulty lies in the fact that these two conditions are often associated at one time in the same patient. The difference between the clinical aspect of jaundice resulting from sudden blockage of the common duct by an impacted stone, and jaundice associated with acute toxic atrophy of the liver, can be readily appreciated. In cases, however, where the obstruction is painless or where the toxicity is mild, the differentiation may be difficult. In toxic or infectious hepatitis there is practically always an element of obstruction due to blockage of the small ducts and canaliculi by cell debris and inflammatory exudate. Prolonged occlusion of the liver ducts must inevitably lead to injury to the liver parenchyma as a result of back pressure and to an interference with the function of the secreting cells. In both instances whole bile is regurgitated into the blood stream. The end result is essentially the same whether we begin with duct occlusion or with toxic injury. It would seem futile, therefore, to expect any one laboratory test, or combination of tests, to consistently differentiate between two conditions which, while theoretically quite different, are actually in the patient so closely interwoven.

The history of the patient and the course of the disease shed more light on the problem than any one procedure. The family physician, who is often able to observe and study the early manifestations of the disease, has a better opportunity than any one else of arriving at the correct diagnosis. The age of the patient, mode of onset, progress of symptoms and signs, weight changes and type of temperature reaction are all important. One should be informed as to recent and remote illnesses, nature of employment, possible exposure to toxic factors and poisons, drugs taken, respiratory infections, digestive disturbances, and habits of living. Frequently a well-taken history will determine the diagnosis more definitely than complicated laboratory procedures.

Physical examination may reveal more from the general than from the local standpoint, and it is important that the patient be studied as a whole rather than merely as a case of jaundice. Careful search should be made for malignant foci in different parts of the body. Examination of the heart may disclose evidence of congestive heart failure or adhesive pericarditis. Tumor masses may be found in the abdomen or an enlarged spleen may be palpated, pointing to chronic degenerative changes in the liver.

Examination of the liver itself is often helpful. The size of the organ, the degree of tenderness, the character of its edge and surface, in conjunction with the general picture, may give an important clue to the diagnosis. The liver of acute catarrhal jaundice is usually slightly enlarged and soft. With severe toxic degenerative changes, the liver tends to decrease in size, and at times the decrease is very rapid. Carcinomatous nodules may be felt on the surface. If the gall bladder is enlarged and palpable, carcinoma obstructing the duct is probable (Courvosier's

sign). That these signs and symptoms at times may lead us astray is admitted, but on the whole they are more reliable than most of our special tests. It is worth pointing out again that in the large group of conditions producing jaundice of the retention type, a careful general study should reveal the nature of the disease.

Laboratory procedures for the differential diagnosis of obstructive jaundice from jaundice due to liver injury are numerous but on the whole rather disappointing. Of value are studies of the formed elements of the blood, and stool and urine examinations, frequent determination of the quantity of serum bilirubin, the galactose tolerance test, serum protein estimation with the ratio of albumin to globulin, hippuric acid excretion, blood phosphatese, and determination of blood cholesterol, especially the ester fraction.

The leucocyte count, particularly the differential formula, may be of some help. In general, in mild catarrhal jaundice the leucocytes are either normal or decreased with a tendency to a more definite fall in the granulocytes. Even in acute toxic liver injury the tendency is to a low count and in some instances, especially of arsenical poisoning, the blood count may approach that seen in agranulocytosis. On the other hand, in obstructive lesions associated with infection of the ducts, both the total leucocyte count and the percentage of granulocytes are usually increased.

Careful daily observations of the amount of bile pigment in the stool may throw considerable light on the cause of jaundice in a given case. The absence of pigment in the stools is indicative, of course, of complete biliary obstruction. If bile pigment is absent from the stools for a considerable period of time, carcinoma of the head of the pancreas is probable. A stone in the common duct usually does not cause complete obstruction. In catarrhal and toxic jaundice, while the obstruction may be complete for a time, it rarely remains so over a long period.

Considerable information is to be gained from examination of the urine. In pure retention jaundice bilirubin may not appear in the urine until late, but with regurgitant jaundice it will spill over at a much lower level, and in this instance bile salts will also be present. The presence of urobilin in the urine is of considerable consequence. Bilirubin excreted into the intestines is changed into urobilin by bacterial action. This urobilin is absorbed and in the presence of a normal liver is again excreted. However, if liver damage is present it accumulates in the blood and finds outlet through the kidney. In hemolytic jaundice there is an excessive formation of urobilin due to an increased amount of bile in the stools. This substance, therefore, has a higher level in the blood and part of it escapes in the urine. The presence of urobilin in the urine then means one of two things: either an excessive production of bile pigment (hemolytic jaundice), or damage to the liver cells without complete obstruction. An exception may be noted to this where obstruction of the common duct exists together with an infection of the liver duct, as it has been shown that urobilin may be formed by bacterial action on bilirubin in the ducts themselves.

Quantitative studies of the bile pigment of the blood are of considerable importance. Van den Bergh observed that if the diazo reagent was added to certain sera a color reaction took place, while in other sera the color change was possible only after the addition of alcohol (the so-called direct and indirect reaction). The indirect reaction is given by the retention bilirubin, while the direct reaction occurs when liver bile has been regurgitated into the blood stream. It is of no value in differentiating between obstructive jaundice and jaundice due to liver injury except at the very onset of an attack. In acute obstruction of the common duct, retention of bile develops very rapidly and within five to six hours a back flow of bile into the blood stream occurs. With this established, a direct Van den Bergh reaction develops and remains positive as long as the obstruction exists. In jaundice of hepatic origin the development of a direct Van den Bergh occurs more slowly and there is a longer period during which the reaction is either indirect or biphasic.

The quantitative Van den Bergh enables one to follow accurately the various changes in the level of bilirubin in the serum. It is a more accurate index of the level of jaundice than the icterus index of Meulengracht. The latter method merely records the relative degree of yellow color in the serum as compared to a standard 1-10,000 solution of potassium bichromate. Its accuracy is affected by cloudiness of the serum, presence of hemolysis, and the occurrence of other yellow pigments in the serum. Furthermore, the indirect type of bilirubin has a lower color value than the direct type, and the icterus index does not reflect the actual level of jaundice.

Observation of the changes in the daily level of

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serum bilirubin gives considerable insight into the nature of the pathological lesion. Obstruction due to carcinoma of the head of the pancreas gives a steadily rising curve without remission, whereas obstruction due to a stone is likely to show considerable variation from time to time and rarely reaches a very high level. Partial obstruction from stricture will often be characterized by a rather flat curve at not an excessively high level. In acute hepatic degeneration, a high level of bilirubin is associated with evidence of severe toxicity, and a rapid downward course, or in the milder catarrhal cases with a tendency to recession.

The galactose tolerance test introduced by Bauer is based on the fact that galactose is converted into glycogen by the normal liver and that there is no fixed renal threshold for galactose. If forty grams of galactose is fed to an individual with a normal liver and without disturbance of carbohydrate metabolism, only a small fraction, three grams or less, will be excreted by the kidneys over a period of five hours. If extensive damage to the liver exists, conversion of galactose into glycogen will be interfered with and consequently a larger proportion will be found in the urine. While the results of the test are subject to considerable variation, a marked increase in the amount of galactose excreted points to definite liver damage. In obstructive jaundice, particularly in the early stage, the test is negative and it may thus serve to differentiate between obstructive and hepatic jaundice.

The level of blood phosphatese may be of differential importance. Elevation above 35 units points to an obstructive lesion, while values below 10 units are indicative of severe liver damage. Unfortunately, intermediate values are frequently found and are of little aid in diagnosis.

Extensive injury to liver tissue, either acute or chronic, may result in a fall in the serum protein and especially in the albumin fraction. This fall may be of a considerable degree and thus become a factor in the development of edema and ascites.

Cholecystography is of little diagnostic aid since in any condition associated with jaundice the passage of the dye through the liver is greatly delayed. Flat plates of the abdomen may be useful in revealing stones, either in the gall bladder or in the biliary ducts.

The hippuric acid test is based on the power of the liver to combine benzoic acid and glycin to form hippuric acid. With injury to the liver cells this function is impaired and the excretion of hippuric acid in the urine is quantitatively affected. Unfortunately, the excretion of hippuric acid is delayed where renal damage exists and the test is thus only of value where renal function is unimpaired.

No conclusive statement can be made regarding the blood cholesterol level in hepatic disease. While the generally accepted normal level of blood cholesterol is 150-200 mg. per 100 cc., this is subject to considerable variation in health and disease. There is a tendency to hypocholesteremia in hyperthyroidism and in all diseases associated with excessive wasting, while in hypothyroidism, lipoid nephrosis, and diabetes mellitus, there is a marked increase. The level is also considerably affected by dietary factors. In general, in acute toxic degenerative conditions of the liver there is a tendency to hypocholesteremia, while in obstructive lesions without extreme liver damage hypercholesteremia may be present. Of more importance is the variation in the cholesterol esters. Normally, from 40 to 70 per cent of the total cholesterol is in combination with fatty acids. An enzyme esterase is present in the liver and it seems probable that a constant process of building up cholesterol esters and of splitting these products into cholesterol and fatty acids is going on. In severe liver injury this process is interfered with and the percentage of cholesterol esters as compared with the total cholesterol falls rapidly, so that in advanced liver degeneration the esters may be almost absent. Low values for cholesterol esters are found in cases with severe degenerative lesion of the liver, whereas in obstructive jaundice without advanced damage to the liver, the esters remain normal or are increased. Interpretation of the level of cholesterol and cholesterol esters must be made in the light of our knowledge of other factors that affect their concentration in the blood.

Treatment of jaundice is the treatment of the underlying condition, of which the jaundice is merely a prominent symptom. It follows then that effective treatment can be planned only after adequate diagnostic study. Each condition associated with hemolysis of the erythrocytes and with jaundice of the retention type has a fairly characteristic clinical picture. Adequate study will, in most instances, reveal the nature of the condition. Treatment appropriate to the particular disease can then be instituted.

In those cases due to obstruction of the common

duct, the treatment is essentially surgical. It is not so important to make a definite diagnosis as to the cause of the obstruction as it is to establish the fact of obstruction. Since there is no medical treatment for these cases as an alternative to surgery, exploratory operation should be undertaken as soon as one is satisfied that one is dealing with obstructive jaundice, unless it is quite clear that the obstruction lesion is of such a nature that surgery can offer no relief. As has been pointed out, prolonged obstruction leads to progressive degenerative changes in the liver, and for this reason it is important that surgical intervention, when indicated, should not be delayed. It is further to be emphasized that in the early stage of obstruction, before degenerative lesions have developed, the differential diagnosis can be made with more certainty.

Surgical intervention in jaundiced patients has in the past often been delayed on account of the marked hemorrhagic tendency of certain of these patients and the absence of any satisfactory method of determining which patients would bleed or of controlling excessive bleeding in those that showed a tendency to hemorrhage. Recent developments in our knowledge of the relationship of vitamin K deficiency to prothrombin deficiency has thrown a new light on the problem of hemorrhage in jaundiced patients. It is now known that individuals with jaundice show a variable degree of deficiency of prothrombin in their blood. If this deficiency reaches a certain critical level, a hemorrhagic tendency exists, or hemorrhage may develop spontaneously. Practical laboratory methods are now available for determining the level of prothrombin. If the prothrombin time is dangerously prolonged, it is now possible to correct this condition by the administration of adequate amounts of vitamin K in conjunction with bile salts. Thus one of the principal deterrents to surgery in jaundiced patients has been removed and we can more freely advise exploration when the diagnosis is in doubt.

The considerable group of jaundice cases in which the condition is due to toxic or infectious injury to the liver cells is the subject of medical treatment. These cases may vary in severity from a mild catarrhal jaundice of little consequence to a fulminating type of acute yellow atrophy. Medical treatment practically resolves itself into two principal procedures; first, elimination, if possible, of the primary cause of the liver injury, and, second, the maintenance of a high carbohydrated intake. It has been abundantly shown that the liver cells are protected to a degree from the toxic action of certain substances if the glycogen content of the liver is maintained, and, further, that regeneration of damaged liver tissue proceeds more rapidly in the presence of an adequate carbohydrate and protein intake. The necessary carbohydrate may be supplied by mouth, if possible. If an adequate amount is not taken orally, sufficient additional carbohydrate in the form of glucose to make up a total intake of at least 200 grams in twenty-four hours should be given intravenously or subcutaneously. Fats should be restricted to the amount necessary to make the food palatable. In the absence of bile salts from the intestine, absorption of fat is interfered with and an excess of fat becomes a burden on digestion without benefiting the patient. Another factor of considerable importance in producing and prolonging liver injury is anemia. Rich has pointed out that anoxemia is implicated in the development of jaundice of the retention type associated with the hemolytic diseases. This state of anoxemia may be partly relieved by the use of oxygen, but perhaps can better be controlled by correction of the anemia. Since severe liver damage, especially of the chronic type, may interfere with storage of the anti-anemic substance, it is not unusual to encounter an anemia of the macrocytic type responsive to liver extract. In other types of anemia transfusion and iron are indicated. General measures to provide rest, sedation, a free intake of fluid, and regulation of the bowels should be employed. Active catharsis should be avoided. These patients are already depressed, both physically and mentally, by their disease. Why add to their misery? These various measures, even in cases of severe liver injury, are often rewarded by remarkable results.

Seven years ago a man, age forty-one, was exposed to fumes from a brass foundry. He developed severe chills and high fever, rapidly followed by jaundice, nausea, vomiting, delirium, and coma. The serum bilirubin reached a concentration of 25 mg. per 100 cc. The urine output was very scanty and the urine showed a large amount of albumin, with many red blood cells and casts. The non-protein nitrogen of the blood rose to 181 mg. and the creatinine to 7.8 mg. Following active treatment with large amounts of fluid and adequate intravenous glucose, this patient made a complete recovery and today has no demonstrable liver impairment.

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CONCLUSIONS

1. An understanding of jaundice requires a clear appreciation of the factors concerned in the formation of bilirubin and its elimination by the liver.

2. Retention jaundice is primarily related to the specific diseases causing an increased destruction of red blood cells, and secondarily to injury of the liver cells.

3. Differentiation of obstructive jaundice and jaundice due to liver injury is difficult but is of the first importance.

4. Diagnosis must be based on a consideration of all the facts gathered from the history, physical examination, and laboratory studies. There is no single laboratory method of making a satisfactory diagnosis.

5. Adequate carbohydrate and protein intake is a most valuable aid in the medical treatment of degenerative liver injury.

339 Boush Street.

THE USE OF SULFANILAMIDE POWDER IN OPEN WOUNDS.*

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and
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This article is written to give our experience in the use of sulfanilamide powder in open wounds.

We started using sulfanilamide powder at the Lewis-Gale Hospital on December 1, 1939, and by May 1, 1940, we had used it in two hundred and seventy-three cases in the industrial department.

We have treated wounds about the scalp, face and hands in the usual manner as to cleansing and antiseptics, doing debridement and inserting sutures, only one change being made,—that is, leaving drains out of the wounds. In most cases, sulfanilamide powder, which has previously been autoclaved, is gently sprayed from an atomizer, used as a blower, over the wounds. Where there is any depth to the wound, and in puncture wounds, sulfanilamide powder on the end of a curet is carried the depth of the wound. In the irrigation of cavities, sulfanilamide powder, suspended in water in a rather thick solution, is used.

Several cases are herewith mentioned to demonstrate the ways in which we have used sulfanilamide powder.

Case I. Compound fracture of pelvis. This case formed an abscess in November. In December, the use of 16 cc. of sulfanilamide powder daily in the abscess cavity was started. A blood test for sulfanilamide on February 3, 1940, showed .4 mg. per 100 cc. of blood. There has never been any cyanosis of this patient's fingers, nails or lips, nor any untoward development from the use of an excessive amount of sulfanilamide powder.

Case II. Deep abscess of sole of foot, following an X-ray burn of twenty years' standing. This case developed an abscess, the depth of which was over 2.2 cm. The wound was packed daily for three weeks with approximately .3 gms. of sulfanilamide powder. A blood test for sulfanilamide on February 7, 1940, when the wound was nearly healed, showed no evidence of sulfanilamide poisoning. At the present time this wound is healed.

Case III. Cellulitis and osteomyelitis of the left fourth metatarsal bone from an old nail puncture wound. The wound was curetted and packed with sulfanilamide powder daily for a period of three weeks. The wound is now entirely healed. Blood tests showed no abnormality.

Case IV. On January 7, 1940, a patient was admitted to the hospital with a compound fracture of the inferior maxilla. There was a wound near the tip of the right side of the chin, through which the bone was protruding. The wound was so large that the index finger could be carried through the wound to aid in reduction of the fracture. The wound was given the usual treatment as to cleansing with antiseptics. Sulfanilamide powder on a gauze sponge was scrubbed into the soft tissues of the compound wound, and the wound was closed without a drain. In ten days the sutures were removed. Examination revealed primary union of the soft tissues, and there was only a faint scar noticeable.

*Read before the Staff Meeting of Lewis-Gale Hospital, Roanoke, Va., May 1, 1940.

Case V. Compound, comminuted fracture of left leg. This patient was admitted to the hospital on January 28, 1940. The upper fragment of the tibia extended through the skin for a distance of over 4.4 cm. The leg was shaved and the wound was washed thoroughly with liters of water; the usual antiseptics were used. The leg was then opened further, and sulfanilamide powder was sprayed over the bone before the bone was carried into the leg. After the bones were in position for a bone plate, sulfanilamide powder was again sprayed. After the plate was applied, sulfanilamide powder was sprayed. The wound was closed without a drain, and a cast was applied. The patient left the hospital on February 3, 1940, at which time his temperature was normal, and primary union of the soft tissues had taken place.

Case VI. On February 1, 1940, a patient was admitted to the out-patient department of the hospital with a 13.2 cm. wound on the palmar surface of the right forearm. The tendons were exposed and the wound was bleeding profusely. The wound was treated in the usual manner, and sulfanilamide powder was sprayed down among the tendons. The wound was closed without a drain. Primary union occurred within ten days.

Case VII. A child came in with nose almost completely severed from the face, it being attached only by the columna. This wound was thoroughly cleansed with water and antiseptics. Sulfanilamide powder was rubbed into the wound, which was then closed without a drain. In one week the sutures were removed, and the wound was entirely healed by primary intention (see illustration—Fig. 1, A and B).

Case VIII. A white female, aged thirty-two, was admitted to the hospital following an explosion of a cook stove on January 19, 1940, at which time she sustained a ragged, lacerated wound extending from the bridge of the nose across the forehead to a little beyond the hair margin on the right side; a badly comminuted, depressed fracture of the frontal bones; and a large opening into the nasal cavity through the ethmoid sinus. This fracture involved the entire right frontal sinus. Numerous pieces of bone were driven into the brain substance and there was a loss of approximately 15 cc. of brain tissue from the right frontal lobe. There was a large third degree burn on the left thigh.

Fig. 1, A and B.

Under local anesthesia, the depressed portions of the frontal bone were lifted into as good position as possible. Several of the loose particles of bone which were driven into the brain were removed, leaving a defect in the frontal bone about 4.4 cm. long and 1.1 cm. wide. Debridement was done on the lacerated wound, a liberal quantity of sulfanilamide powder was placed in the wound, skin edges were approximated with silk sutures, and a small rubber dam drain was inserted down to the opening in the dura. The wound healed without infection, and the patient was discharged from the hospital on February 21, 1940, symptom-free.

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Fig. 2, A and B.

Case IX. A young male, aged twenty-one, was admitted to the hospital on February 27, 1940, following a motorcycle and truck accident. He had a crushing injury of the face consisting of a ragged, lacerated wound beginning on the left side of the nose, and extending through the entire thickness of the nose and right upper lip. This wound dissected out over the right side of the cheek, and the lip was torn loose from the alveolar process from the midline to the second molar. The nasal bones and the right maxilla were crushed, and there was a fracture through the right side of the inferior maxilla.

The wounds were cleansed and the right antrum was packed tightly with gauze in order to hold this crushed bone in as nearly normal position as possible. A strip of gauze was also inserted into each side of the nose in order to hold these tissues in approximately normal position. The wound was liberally sprinkled with sulfanilamide powder, and sulfanilamide powder was placed on the gauze which was in-

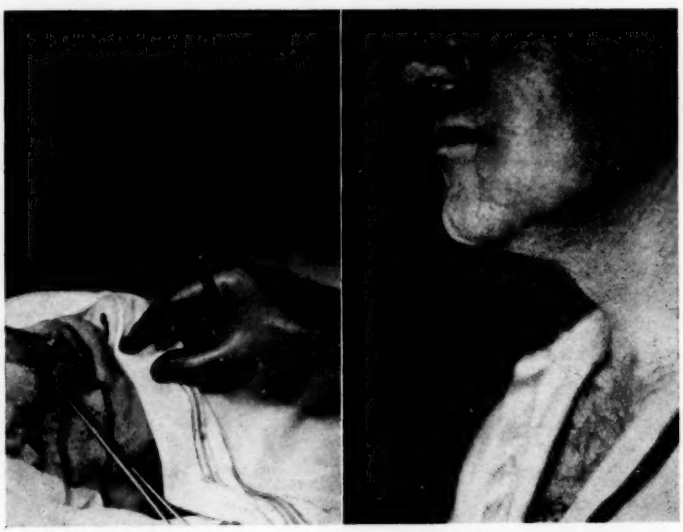

Fig. 3, A and B.

serted in the right antrum and nose. The wounds were sutured without drains. Later the teeth were wired into occlusion. The wound healed by primary intention, and the sutures were removed on the fifth post-operative day. All dressings were discontinued on the seventh post-operative day (see illustration—Fig. 2, A and B).

Case X. A white male, aged thirty-three years, was admitted to the hospital on April 22, 1940. He had a ragged, lacerated wound beginning at the angle of the mouth on the left side at the vermilion border and extending downward about 4.4 cm. This wound extended through the entire thickness of the lip and there was some damage to the periosteum of the inferior maxilla. There was no evidence of fracture. The portion of the wound involving the mucous membrane covered an area about 3.5 cm. by 1.5 cm.

Under novocain anesthesia the wound was cleansed and debridement done; wound was sprinkled with sulfanilamide powder. The wound on the mucous membrane was closed with catgut sutures, and skin was closed with dermal sutures. No drain was used. The wound healed by primary intention in ten days (see illustration—Fig. 3, A and B).

It was observed that after sulfanilamide powder had been used on minor wounds that were bleeding freely, there was a tendency for the bleeding to decrease.

Although the wounds treated have ranged from those of a minor nature to very serious ones, practically all of them have been closed without drains. Sulfanilamide powder has been sprayed, rubbed and packed into the wounds. So far no ill effects have ensued, and the patients have convalesced without incident. We had previously thought that no traumatic wound, no matter how thoroughly it was cleansed, should be closed without the use of a drain for at least twenty-four hours.

We believe, from our experience, that the use of sulfanilamide powder in wounds is of distinct advantage.

THE RESULTS OF TREATMENT OF MALIGNANT TUMORS OF THE LARYNX, HYPOPHARYNX, NASOPHARYNX, AND SINUSES.*

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and
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Our present methods of treatment of malignant tumors have been in use for the past seven years, and this report is the result of a detailed study of fifty cases, in whom the objectives of treatment were completely carried out and our follow-up records were likewise complete.

All case records which could not meet these requirements were omitted. Correct data must be available to evaluate results and draw conclusions to guide us in the future.

The organization of the McIntire Tumor Clinic has been a great factor in taking care of this ever increasing problem by furnishing the material set-up necessary to supervise the attendance of patients and their follow-up records, as well as radium and X-ray equipment and the hospitalization of indigent patients within its means. The second great advantage of an organized tumor clinic is in the attendance of the hospital staff for consultation and discussion, so that when treatment is planned for each particular case, it will meet with the approval of the best opinion available.

The growth of the Tumor Clinic has been rapid, and today it has an average attendance of about twenty patients, with approximately 450 new patients availing themselves of its services last year. The methods of modern treatment are necessarily crude; but until some specific remedy appears, in the form of a new chemotherapeutic drug or serum or whatnot, we must rely on surgery, radium, and X-ray, either alone or in combination.

It is in the choice of these weapons that the group conference becomes important.

When one accepts the responsibility of taking care

*Read before the Virginia Society of Ophthalmology and Oto-Laryngology, Old Point Comfort, Va., May 18, 1940.

From the Departments of Oto-Laryngology and Radiology, University of Virginia Department of Medicine, Charlottesville, Va.

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of a patient with a malignant tumor, he should not only possess the surgical skill which may be necessary, but also possess a broad knowledge of radiation therapy and the probable results which can be expected. It is with this end in view that we have summarized our experience to serve as a guide for all who are interested in this subject, with the hope that they will profit thereby.

To consider all the malignant tumors in the field of otolaryngology would be too time consuming, so we have restricted this study to the four areas mentioned in the title, and have tabulated the results in each group.

Early diagnosis is of first importance in the fight against this dread disease, and constant vigilance on the part of the physician and education of the public in the recognition of early symptoms and signs is the best method of obtaining this end.

A competent and adequate department of Pathology is next in importance, for treatment is guided by the knowledge of the type and grade of malignancy of the tumor.

Competent surgeons and radiologists with adequate equipment at their disposal along with facilities for hospitalization, especially for the indigent, is next in importance.

The State has been negligent in providing these things for a disease which is fast climbing to the forefront of our mortality tables. Considering the amount of money furnished for the prevention and treatment of tuberculosis and for other public health measures, it is astounding to see how little is provided for the prevention and treatment of malignant tumors. This condition can and should be remedied.

TABLE I

EARLY INTRINSIC EPIDERMOID CARCINOMA OF THE LARYNX. TREATED BY LARYNGO FISSURE AND LOCAL EXCISION.

AGE	GRADE	DURATION SYMPTOMS	RESULT
59	II	2 mo.	Well ½ year
69	I	3 mo.	Well 1½ year
61	I	1½ mo.	Dead 2 years—Ca. lower esophagus.

Out of the twenty-three cancers of the larynx included in this study, only three were seen early enough to be treated by the simple procedure of opening the larynx and excising the tumor locally. They had all presented a prominent symptom, hoarseness, for from one and one-half to twenty-four months, with an average of six months, before a diagnosis was made. Since surgery offers a cure in the large majority of early cancers of the larynx, since the tumor is easily seen with a mirror, since these tumors metastasize late, since the early symptom of hoarseness is present and the voice can be saved, there is no excuse for such delay.

Any patient with a persistent hoarseness should have a laryngeal examination.

Radiation therapy is not indicated in this group, under present circumstances, and surgical removal should always be advised and employed.

Two of these patients are living and well after one-half and one and one-half years, respectively. The other patient showed no evidence of local recurrence, but died from a second highly malignant tumor of the lower end of the esophagus two years after operation.

TABLE II

ADVANCED INTRINSIC EPIDERMOID CARCINOMA OF THE LARYNX. TREATED BY TOTAL LARYNGECTOMY.

AGE	GRADE	DURATION SYMPTOMS	RESULT
73	II	7 mo.	Well ½ year
39	II	3 mo.	Well 1 year
48	II	7 mo.	Well 1 year
57	II	12 mo.	Well 2½ years
59	I	6 mo.	Well 3½ years
52	II	3 mo.	Well 5 years
46	I	24 mo.	Well 5 years
54	III	1½ mo.	Well 7 years
54	II	4 mo.	Well 7½ years
58	III	7 mo.	Dead 2 days—Heart
53	III-IV	2 mo.	Dead 1½ years—Ca. lower trachea.

Eleven patients presented an intrinsic tumor too far advanced for local excision, so complete removal of the larynx was done. Surgery again offers the best chance of cure, and radiation should not be advised in this group. Nine of these patients are alive and well after from one-half year to seven and one-half years. One died a cardiac death on the second day, and one from a second tumor which arose in the lower trachea, producing death one and one-half years after operation.

These people are happy and carrying on their work in a normal manner. The loss of their voice is compensated for, either by the development of a buccal voice, or by an artificial larynx. The mortality to date in these two groups is approximately 14 per cent.

A group of four patients who presented advanced cancer of the larynx, with extension into the regional

TABLE III

ADVANCED EXTRINSIC EPIDERMOID CARCINOMA OF THE LARYNX. TREATED BY TRACHEOTOMY AND X-RAY RADIATION.

AGE	GRADE	DURATION SYMPTOMS	RESULT
59	III	5 mo.	Dead 17 days—Heart.
64	II	2 mo.	Dead 2 mo.—Lung abscess and pneumonia.
68	III	5 mo.	Dead 2 mo.—Lung abscess, pneumonia and empyema.
63	III	12 mo.	Dead 3 mo.—Lung abscess, pneumonia and empyema.

nodes and neck, were obviously incurable by surgery; so tracheotomy was done and treatment was carried out by X-ray radiation. One died a cardiac death on the seventeenth day; the other three survived for from two to three months and died from lung suppuration, pneumonia and empyema; so we discontinued this method of therapy, because, when suppuration occurred in the larynx, aspiration soon followed. The mortality rate here was 100 per cent.

TABLE IV

ADVANCED EXTRINSIC EPIDERMOID CARCINOMA OF THE LARYNX. TREATED BY TOTAL LARYNGECTOMY AND X-RAY RADIATION.

AGE	GRADE	DURATION SYMPTOMS	RESULT	
53	III	12 mo.	Well 2½ years	
62	II-III	6 mo.	Dead 1 mo.	—Metastasis lung
52	II	6 mo.	Dead 8 mo.	—Metastasis lung
49	II	6 mo.	Dead 1⅓ years	—Metastasis lung
59	II-III	2 mo.	Dead 2½ years	—Metastasis lung

Because of our unhappy experience with the group in Table III, we felt that if the larynx was removed, disregarding tumor, the neck could be radiated with impunity as far as suppuration and aspiration were concerned; so a group of five patients were treated in this manner, and we feel that it represents a step forward in the treatment of these advanced cases. Four subsequently died from cancer of the lung; but they survived one month, eight months, one and one-third years, and two and one-half years, respectively; and one is alive and well two and one-half years after treatment. The mortality to date in this group is 80 per cent.

We do not feel that cancer of the hypopharynx is amenable to surgical treatment. These lesions were above the cords and involved the aryepiglottic folds, the epiglottis, the pyriform sinus, and at times the lateral pharyngeal wall. The tumor was locally excised by a coagulating current and the base planted with radon seeds in two instances; X-ray therapy then followed. Radium and X-ray were used in two, and X-ray alone in one. One of these patients is well and apparently free of disease after seven months. Two others received apparent cures in that they died from heart disease four and one-half and five and one-half years after treatment. There was no apparent evidence of cancer at the time of death. The last two survived for one and one-half months and two and one-half years respectively, but died as a result of the disease. These results are very encouraging. The mortality in this group was 40 per cent.

The presence of a malignant node in the neck, especially when associated with ear symptoms, should always lead to a careful inspection of the nasopharynx as a site for the primary tumor; but many such tumors are found before the regional nodes become involved. Among our group of six cases, four were transitional cell carcinomata. Of these one died a cardiac death and one from pneumonia. Two are still living after seven months and one and one-half years respectively, with no evidence of tumor today. Two were epidermoid carcinomata; one is alive and apparently well after one and one-half years, and

TABLE V

EPIDERMOID CARCINOMA OF THE HYPOPHARYNX.

AGE	GRADE	DURATION SYMPTOMS	PROCEDURE	RESULT
78	III	1 mo.	Radon and X-Ray	Well 7 mo.
55	II	6 mo.	X-Ray	Dead 1½ mo.—Carcinoma
70	II	4 mo.	Local excision Radon and X-Ray	Dead 2½ years—Carcinoma
65	III	4 mo.	Radon and X-Ray	Dead 4½ years—Heart
63	III	8 mo.	Local excision Radon and X-Ray	Dead 5½ years—Heart

TABLE VI
MALIGNANT TUMORS OF THE NASOPHARYNX.

AGE	GRADE	DURATION SYMPTOMS	REGIONAL NODES	PROCEDURE	RESULT
16	Trans.	2 mo.	No	Local excision and X-Ray	Well 7 mo.
56	Epi. Ca. III	12 mo.	Yes	X-Ray	Well 1½ yrs.
60	Trans.	½ mo.	Yes	Local excision and X-Ray	Well 1½ yrs.
25	Sarcoma	1 mo.	No	X-Ray	Well 4½ yrs.
23	Trans. III	8 mo.	Yes	X-Ray	Dead 2 mo.—Pneumonia
66	Trans. I & II	6 mo.	Yes	X-Ray	Dead—Heart
60	Sarcoma	1 mo.	Yes	X-Ray	Dead 6 mo.—Metas. lung
80	Epi. Ca. II	10 mo.	No	Radon	Dead 1 yr.—Metas. brain

the other died from a brain metastasis in one year. The last two were sarcomata, of which one died from pulmonary metastasis in six months, and the other one is alive and apparently well after four and one-half years. Among this group we have only a 50 per cent mortality to date.

Advanced cancer of the sinuses presents a big problem, for in practically every instance the growth has invaded adjacent sinuses and other structures. In this table are five transitional cell carcinomata. One is alive and apparently well after two years. The other four lived one and one-half months and one and one-third, two and three and one-half years, respectively, before succumbing to metastases of the brain, or, in the latter case, to a probable second tumor of the kidney. The site of the original tumor here was still clear, and it is difficult to think of a metastasis after so long a time. The mortality in this group is 80 per cent, but the results on the whole are encouraging.

Nine tumors of the sinuses were epidermoid carcinomata, and the results from radiation therapy were all most discouraging. One hundred per cent are dead, and the longest survival was only thirteen months; so we have concluded that in the future these tumors should be treated surgically, in spite of the mutilating procedure which must be done.

As for the cervical gland metastases, we are still in somewhat of a quandary as to whether X-ray radiation is best or block dissection of the neck. We are inclined to advocate the latter, especially in those tumors of a low grade of malignancy.

TABLE VII
ADVANCED CARCINOMA MAXILLARY SINUS AND ADJACENT STRUCTURES.

AGE	GRADE	REGIONAL GLANDS	DURATION SYMPTOMS	PRECEDING OPERATIONS	PROCEDURE	RESULT
78	Trans. III	No	4 mo.	No	Ext. local excision and X-Ray	Well 2 yrs.
65	Trans. III	Yes	6 mo.	No	X-Ray	Dead 1½ mo.—Brain
72	Trans. III	Yes	7 mo.	Local op. 7 mo. ago	Radium and X-Ray	Dead 1⅛ yrs.—Brain
30	Trans.	Yes	1 mo.	No	X-Ray	Dead 2 yrs.—Brain
60	Trans.	No	2 mo.	No	X-Ray	Dead 3½ yrs.—Ca. Kidney and abdomen

TABLE VIII
ADVANCED CARCINOMA MAXILLARY SINUS AND ADJACENT STRUCTURES.

AGE	GRADE	REGIONAL GLANDS	DURATION SYMPTOMS	PRECEDING OPERATIONS	PROCEDURE	RESULT
55	Epi. II	No	6 mo.	Tooth Extraction	X-Ray	Dead 1 mo.—Pneumonia
82	Epi.	No	1 mo.	No	Radium and X-Ray	Dead 3 mo.
65	Epi. II	No	1½ mo.	No	Ext. op., local excision and X-Ray	Dead 4 mo.
42	Epi. III	Yes	10 mo.	Intranasal Operation	X-Ray	Dead 4 mo.
38	Epi. II	No	1½ mo.	No	X-Ray	Dead 5 mo.
52	Epi. III	No	8 mo.	No	X-Ray	Dead 6 mo.
40	Epi. II	Yes	3 mo.	Intranasal Operation	X-Ray	Dead 6 mo.
75	Epi. I-II	No	6 mo.	No	X-Ray	Dead 6 mo.—Brain
42	Epi. III	No	2 mo.	Tooth Extraction	X-Ray	Dead 13 mo.

CONCLUSIONS

1. Intrinsic cancer of the larynx should be treated surgically.

2. Extrinsic cancer of the larynx should have a preliminary laryngectomy, disregarding neck extension, followed by X-ray therapy.

3. Cancer of the hypopharynx is best treated by a combination of methods, relying chiefly on X-ray

radiation, but employing in certain cases local excision or radon implantation, or both, as a preliminary step.

4. Malignant tumors of the nasopharynx are again best treated by X-ray radiation with an occasional carotid ligation, local excision and/or radon implantation as a preliminary step.

5. Transitional cell carcinomata of the sinuses may well be treated by X-ray radiation; but the eye must be sacrified on the same side, for, in order to prevent early brain metastases, the area of treatment must reach to the base of the skull.

6. Epidermoid carcinomata of the sinuses are best treated surgically, perhaps depending on X-ray radiation to handle cervical metastases, especially in the more highly malignant tumors, and perhaps block dissection in the others.

As a result of our experience with radiation therapy, numerous observations have been made which may be briefly enumerated as follows:

1. X-ray therapy must be given up to toleration of the patient through adequate portals.

2. It is well to remove carious and septic teeth before starting treatment.

3. Always remove metallic objects adjacent to the field, such as tracheotomy tubes and jewelry, to avoid the effects of secondary radiation.

4. The reacting skin should be left alone, keeping it dry with the aid of zinc stearate dusting powder, and left exposed to the air. All clothing should be kept away.

5. Discomfort and pain are best controlled by aspirin and codeine. No bromides should be given.

6. Watch for edema of the glottis; if imminent, the patient should be hospitalized and an emergency tracheotomy set kept at the bedside.

7. Follow the white cell count. If the count falls below 3000, watch, and wait, and transfuse, if necessary. The red count and hemoglobin content are of less importance, but should also be followed.

8. Watch fluid intake. Use intravenous infusions or a nasal tube, if necessary.

9. A high caloric diet with adequate vitamine content should be prescribed.

10. Watch for pneumonia or pulmonary infection.

11. Atrophy of salivary or lacrimal glands is permanent when they are included in the field.

12. We have noted no ill effects to the pituitary or thyroid glands or to the brain.

13. We have noted no ill effects to any of the cranial nerves.

14. Alopecia is usually permanent.

15. Approximately 20 per cent of the nasopharyngeal malignancies develop necrosis of the mandible. Surgical resection of the jaw is indicated when this occurs.

16. When the eye is included in the field, trichiasis is bothersome, but glaucoma and ulceration usually necessitate enucleation.

SUMMARY

In spite of the crude weapons at our disposal today, the treatment of malignant tumors is by no means hopeless, and with adequate State support and constant education of the physician and public, even better results should be obtained year by year.

THE TREATMENT OF NAUSEA AND VOMITING OF PREGNANCY WITH CHLORETONE.

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The treatment of nausea and vomiting of pregnancy has been a problem for the medical profession since its earliest days. Soranus, of Ephesus, about the beginning of the Christian Era, mentioned this disease. Early medical writings show the use of many types of treatment. Bald, in the "Leech Book," which is probably the first medical book composed in the British Isles, written about the latter part of the 9th century, suggests as a quieting drink that might well have been used for this, a combination of betony, helenium, wormwood, ontre, hore-hound, lupin, wen-wort, yarrow, dwarf dwostle, and fieldmore or wild carrot. Simmond in 1813, was the first to do a therapeutic abortion for the condition.

If we could see the patient before pregnancy occurred, many factors, such as foci of infection and organic or functional conditions of the gastro-intestional tract, could be eliminated. Replacement

of the retroverted uterus has often relieved nausea and vomiting. We do not always understand why clearing up a reflex condition such as this helps the cure, but apparently it does. The nervous condition of the patient undoubtedly plays a most important part, and, if psychotherapy can be employed early enough, startling results will often be obtained. There are apparently four factors which govern the treatment of patients with nausea and vomiting: dehydration, starvation, disturbances of carbohydrate metabolism, and nervous exhaustion. The treatment must necessarily take into consideration the severity of the disease, and it goes without saying that the earlier the patient is seen the better are her chances for recovery. Usually when the patient is first seen the toxic and reflex elements can only be partially treated, and we must make the best of what we have to work with. Therefore our biggest problem is to get fluids and solids into the patient and find a way to make her retain them. With this in view, sedation of the so-called vomiting center of the brain and of the gastric mucosa is strived for. It is our purpose to suggest for that an old drug in a new form.

Chloretone or chlorbutanol is an unofficial drug allied to chloral hydrate and occurs in a white crystalline form. It has an odor and taste very much like that of camphor. Due to this, it has been found virtually impossible to give it to patients with nausea already established, although its efficacy has been known for years. It is slightly soluble in cold water but freely so in alcohol. Its physiological actions are local and general: locally, it serves as an anesthetic; its general action is to depress the central nervous system. The dose of chloretone is 2 to 20 grains, the average being 10 to 15 grains for hypnosis and 2 to 15 grains for gastric sedation. In large doses, sleep followed by profound torpor may result. The circulation is little affected, and the absorption is fairly rapid, but elimination is slow. Occasional headache and giddiness follow its administration in large doses.

We are now using a preparation known as "Meredyne," with the following make-up:

℞ Alcohol	2 c.c.
Chloretone	3 grains
Oleoresin of capsicum	.006 grain
Saccharin	.6 grain
Vanillin	.5 grain
Water q.s.	4 c.c.

In this the dosage of chloretone is quite small and can be safely repeated four or five times in twenty-four hours. The taste is not disagreeable and a warming sensation is noticed following its ingestion, due, of course, to the capsicum. The capsicum also tends to stimulate the flow of the gastric juices, especially the acid, which is so badly needed at this time. We find this is best given in about one-third glass of water or sweet milk.

Our routine has been to give the patient suffering with nausea and vomiting a complete physical examination if possible, and foci of infection are eradicated if it can be done. Frequent feedings, high in carbohydrate, are insisted upon. Mild laxatives are used until good elimination is established, and, of course, a frank discussion of the condition is always resorted to. Finally, the chloretone mixture is ordered every four hours while the patient is awake, and she is advised to decrease the frequency of the dosage as soon as possible.

Of twenty cases of nausea and vomiting of pregnancy—ranging from mild to severe, but not true hyperemesis gravidarum—treated in this manner, sixteen showed complete cessation of the nausea and vomiting within three days. Of course, these patients resorted to an occasional dose of the medication at the slightest sign of nausea for periods up to a month. Of the remaining four, three got partial relief in that they were fairly comfortable but had an infrequent attack of vomiting. The fourth of this group took one dose and because of an intense dislike for the flavor of vanilla refused to repeat it. None of these patients complained of dizziness, but three developed slight morning headaches that cleared up in several hours without medication.

SUMMARY

1. Chloretone has been put in a palatable medium and is easily administered.

2. Of twenty cases treated with chloretone, sixteen are classed as cured, three as improved, and one failure.

3. No serious untoward results were noted.

7 South Market Street.

VARIABILITY OF THE BLOOD PRESSURE.*

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Rochester, Minnesota.

Most physicians are not sufficiently aware of the variability of blood pressure. Variations of blood pressure occur both in persons with normal blood pressure and in those with hypertension. In some cases of essential hypertension, the blood pressure may be so variable that on some occasions it is within the normal range; whereas, on other occasions it may be found at very high levels. In a group of cases of essential hypertension it has been demonstrated that the resting blood pressure will average approximately 50 mm. of mercury lower than the first reading which is taken in the office.[1] Failure to give due consideration to this fact has resulted in the dissemination of much confusing information concerning the efficacy of various methods of treating hypertension.

The blood pressure of persons who do not have hypertension also may be quite variable. This variability of the blood pressure in persons with "normal" blood pressure can account for much of the difficulty experienced in determining just what are the limits of normal blood pressure. Some of this difficulty may be obviated by thinking of blood pressure as a measure of a variable physiologic mechanism and by considering the range of variability of the blood pressure of an individual, in addition to the level of the blood pressure at any particular moment. One method of determining the range of blood pressure is to make consecutive readings of blood pressure at hourly or half-hourly intervals for twenty-four to forty-eight hours during periods in which the patient is active and during periods of rest. Another less time-consuming method is to measure the reaction of the blood pressure to a standard stimulus after a basal level of blood pressure has been obtained. The cold pressor test is a satisfactory method for such a determination. The technic of this test has been described in a number of other publications.[4, 5] It consists essentially of measuring the reaction of the blood pressure to a standard cold stimulus. Ayman and Goldshine recently have described a test which they call "the breath-holding test" and which they consider to be a standard test for measuring the reaction of the blood pressure. They have made a preliminary report of their experience with this test but its general use must await information covering the response of a large group of subjects. In my experience, the fact that the subject has had to take an active part in the test, has made it more difficult to standardize than the cold pressor test. However, the breath-holding test does have the advantage of not requiring any special apparatus such as is needed for the cold pressor test.

The majority of subjects with normal blood pressure have a range of variability of approximately 10 to 20 mm. of mercury in systolic pressure and from 5 to 15 mm. in diastolic pressure. Approximately 15 per cent of persons with a usually normal blood pressure will have a range of variability of blood pressure of 20 to 60 mm. of mercury. The variability of the blood pressure in this group of "normal hyperreactors" will be approximately two or three times greater than that of the group of "normal reactors."

The question of the significance of the hyperreactive blood pressure among individuals with usually normal blood pressure is intriguing. In analyzing the results of a study of the reaction of the blood pressure to the cold pressor test in a large group of school children, it was found that the children who were hyperreactors usually came from families in which there was a history of hypertensive cardiovascular disease. This led to the hypothesis that excessive reactions of the blood pressure to a standard stimulus are indicative of a prehypertensive phase of essential hypertension. The following observations with the cold pressor test have helped to confirm this assumption: 1. The hyperreactivity of the blood pressure of the normal hyperreactor is of the same type and frequently of the same degree as that which is characteristic of 95 per cent of individuals with essential hypertension. 2. Individuals who are known to have had hypertension, but whose blood pressure has been reduced to normal by cardiac failure or by other factors, give a hyperreactive response to the cold pressor test similar to that of the person with hypertension. 3. Subjects with usually normal blood pressure, who are hyperreactors, generally come from families in which there is a high incidence of hypertensive cardiovascular disease, whereas subjects with

*Part of Presidential address given at annual meeting of the Ex-Interns Association of St. Elizabeth's Hospital, Richmond, Virginia, October 1, 1939.

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normal blood pressure who are hyporeactors generally do not. 4. Thirty-eight per cent of originally normal hyperreactors have experienced the development of hypertension subsequently, whereas none of the normal hyporeactors have done so.

Other evidence is available which indicates that unusual variability of the blood pressure in persons with usually normal blood pressure is indicative of a prehypertensive state. Robinson and Brucer, following a detailed statistical and clinical study of a large group of persons, have concluded that the normal range of systolic blood pressure is between 90 and 120 mm. of mercury and that the normal range of the diastolic pressure is between 60 and 80 mm. Diehl and Hesdorffer have observed 155 students for a period of seven years and have found that young men showing even transitory elevation of the blood pressure during their college years are much more likely to have an elevated blood pressure after a period of from five to ten years than are students whose blood pressure was consistently within the normal range. The probabilities of their having hypertension in later years was found to be in direct proportion to the frequency of previous elevation of the blood pressure.

In a follow-up study of approximately 1,500 patients with originally normal blood pressures, I have found that the majority (70.4 per cent) of the patients who, as a result of nervous stress, had an original elevation in systolic and diastolic blood pressures into the upper ranges of normal (140 to 150 mm. systolic, and 85 to 100 mm. diastolic) had hypertension subsequently (ten or twenty years later); whereas, only a small number (3.4 per cent) with original blood pressures in the lower ranges or normal had hypertension subsequently.[6] To state this in a different way, of 206 patients who recently had hypertension, 86 per cent gave evidence of hyperreactivity of the mechanism for regulating blood pressure ten to twenty years previously, although they did not have hypertension at that time and the majority did not have hypertension until a number of years had elapsed.

In any consideration of variability of the blood pressure one should distinguish between variability in the systolic pressure and variability in the diastolic pressure, as one does not necessarily have the same significance as the other. The diastolic response is the more reliable index of vasoconstriction. Changes in only the systolic blood pressure are indicative of increased cardiac output, such as may occur with hyperthyroidism, with the effort syndrome, and as a result of the effect of adrenalin. It is probable that excessive variability of the systolic pressure alone is not indicative of subsequent hypertension inasmuch as, in my follow-up study, none of the patients who had an original systolic blood pressure of more than 140 mm. but who had a diastolic blood pressure of less than 85 mm. had hypertension subsequently.

As has been previously stated, the blood pressure of patients who have hypertension varies widely. Mueller and Brown found that these variations are similar to those of patients with normal blood pressure but that the magnitude of the former was about twice as great as that of the latter. It is true clinically that the more severe the hypertension the less closely the blood pressure approaches normal as a result of rest and sleep. Clinical experience indicates that the probability of influencing the blood pressure satisfactorily by any therapeutic procedure is roughly proportional to the tendency for the blood pressure to approach normal as a result of rest, sleep, sedation or anesthesia. There rarely are any symptoms associated with fluctuations of blood pressure in cases of essential hypertension and the patient's chance of predicting the level of his blood pressure accurately is usually no better than if he had guessed. This situation is sharply in contrast to paroxysmal hypertension associated with chromaffin tumors, in which the changes in blood pressure are more abrupt.

The effects on the blood pressure of the immersion in ice water of a hand of a patient with hypertension duplicates roughly the effects of such stimuli as strong emotions and tobacco smoking on the blood pressure. The clinical significance of the sharp increases in blood pressure which result from the application of the cold pressor test is that hypertensive patients have excessive vasoconstriction as a result of hyperirritable sympathico-arteriolar systems.

Paroxysmal changes in blood pressure may result from pheochromocytomas of which about two-thirds are in the suprarenal glands. They affect individuals from sixteen to sixty-nine years of age and cause paroxysms of hypertension as often as several times daily. The episodes of hypertension may last for one to two hours or for only two or three minutes. They occur spontaneously or are induced by physical exertion, sneezing, bending the body in various directions or by pressure on the abdomen. The following symptoms occur during attacks: (1) palpitation (in almost all cases), (2) pain (in about five-sixths of the

cases) which is precordial, epigastric, or located in the head, (3) vomiting (in about two-thirds of the cases), (4) rapid respiration (in about two-thirds of the cases), and (5) sweating (in about three-fourths of the cases). During attacks, the face of the patient becomes pallid or cyanotic. In some instances there is alternate flushing and blanching. Distention of the veins of the neck may occur. Convulsions, chills and fever are absent except that fever may occur shortly before death. The blood pressure is increased during attacks and there may be wave-like variations over a wide range. The pulse rate may increase or decrease, or it may not be changed. Hypertension may be present between attacks (in about half of the cases). The diagnosis is based on the occurrence of characteristic clinical episodes associated with paroxysms of hypertension, palpable abdominal tumor (in half of the cases) and positive roentgenologic findings (in about two-thirds of the cases). Hyperglycemia and glycosuria may occur during paroxysms.

The chief diagnostic difficulty is in distinguishing between episodes of elevation of blood pressure resulting from psychic stimuli and episodes originating from pheochromocytomas. In the former instance, the emotional disturbance is more prominent, and pain, tachycardia, sweating and discoloration of the face are minimal or absent. The elevation of the blood pressure is less marked and there is no physical evidence of tumor.

Orthostatic hypotension is characterized by a fall in blood pressure when the patient assumes an erect position. Ordinarily, the blood pressure rises on assuming the erect position but in cases of orthostatic hypotension, it decreases. The commonest symptom of this condition is weakness on assuming the erect position. Additional symptoms are deficient sweating, failure of pulse rate to increase normally on assumption of the erect posture, accentuation of symptoms in warm weather and excretion of larger amounts of urine when the patient is recumbent than when he is erect.

Various other conditions may cause changes in blood pressure. Holding one's breath or grunting may increase markedly the blood pressure. Pain, fear, excitement, anger and muscular effort almost routinely cause increase in blood pressure and the blood pressure decreases during sleep. Sudden, wide fluctuations in blood pressure may occur with episodes of angina pectoris in cases of lymphosarcoma of the superior mediastinum, in cases of carcinoma of the larynx or esophagus, and in cases of meningitis. Tobacco smoking may cause a marked increase in the blood pressure, especially in the presence of an inherently hyperreactive vascular system. The blood pressure is almost always greater in the leg than it is in the arm. When such is not the case, coarctation of the aorta should be suspected. Blood pressure is unequal in the two arms in about 50 per cent of normal persons; the average inequality in the systolic blood pressure and in the diastolic blood pressure is about 13 mm. of mercury. These differences are not constant but transient, and it is reasonably certain that all people have inequality of blood pressure in the two arms at some time. Naturally, one should suspect organic disease when differences are great and persistent.

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INDUCTION OF OVULATION.

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Associate in Gynecology, Medical College of Virginia,
Richmond, Virginia.

There is now available for clinical use a potent gonadotropic hormone. The substance is derived from the serum of pregnant mares. The ability of this hormone to induce ovulation in the human female with subsequent corpus luteum development can be demonstrated by endometrial biopsy. This is an office procedure, utilizing the suction curet by means of which the endometrium is obtained. Examination of the stained, fixed tissue will reveal the tortuous, enlarged, fluid-filled glands of the endometrium when the specimen is taken several days after ovulation. This paper will report seven cases in which the symptoms could be explained on the basis of ovulation failure, all relieved of their complaint when ovulation was induced.

CASE 1

M. H., age twenty-one. Chief complaint—amenorrhea of eighteen months' duration. Menses were regular until the patient suffered from an acute influenza eighteen months ago, since which time she had not menstruated.

October 13, 1939. Physical examination was negative. B.M.R. plus 10. Weight 116. Pelvic examination showed a nulliparous introitus, intact hymen, cervix small and directed posteriorly, fundus anterior and normal size, tubes and ovaries not palpable. Endometrial biopsy showed an early proliferative phase.

October 20, 1939. Gonadotropic hormone 1 c.c. was given subcutaneously and repeated on the second, fourth, sixth, eighth, ninth, and tenth day.

November 6, 1939. Endometrial biopsy—secretory phase.

November 10, 1939. Menses began and lasted forty-eight hours.

November 16, 1939. Gonadotropic hormone 1 c.c. and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle as based upon the last menses.

November 30, 1939. Endometrial biopsy—secretory phase.

December 8, 1939. Menses began and lasted three days.

CASE 2

M. B., age eighteen, single, virgin. Chief complaint—severe dysmenorrhea since puberty. Menses always regular, flow lasts four days, and the patient was bedridden for the entire period.

August 29, 1939. Physical examination revealed an undernourished white female whose general condition was otherwise negative. B.M.R. plus 15. Weight 102. Pelvic examination—virgin introitus; normal vaginal mucosa; cervix 4 cm. in length; fundus infantile, anterior, and freely movable; right ovary palpable, non-tender, freely movable. Endometrial biopsy proliferative phase.

October 3, 1939. Menses began with severe dysmenorrhea and persisted for four days.

October 25, 1939. Endometrial biopsy—proliferative phase.

November 2, 1939. Menses began with severe dysmenorrhea.

November 8, 1939. Gonadotropic hormone 1 c.c. —repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of cycle.

November 29, 1939. Endometrial biopsy—late secretory phase.

December 1, 1939. Menses began, lasted six days, no pain.

Treatment not instituted during the next month and pain recurred with the next menses. Course of therapy was repeated during the next month with complete relief of symptoms. Since that time ovulation has occurred spontaneously and there has been no dysmenorrhea.

CASE 3

R. N., age twenty-two, white, married three years. Chief complaint—sterility. The menses have always been irregular, varying from two to six week cycles. Libido normal.

June 15, 1939. Examination of the semen showed it to be normal in amount, normal count, active motility, and normal morphology on the stained smear. Pelvic examination was entirely negative with a well-developed uterus. pH of the vaginal secretion was 5.6. Huhner test was negative with fluid aspirated from the cervical canal. Endometrial biopsy taken twenty-five days from the first day of the last menses

showed a poorly-developed proliferative phase. No treatment was instituted until the next menses which appeared on July 20, 1939.

July 26, 1939. Gonadotropic hormone 1 c.c. begun and was repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

August 28, 1939. Menses began and lasted four days.

September 4, 1939. Gonadotropic hormone 1 c.c. and repeated on the eighth, tenth, twelfth, thirteenth and fourteenth day of the cycle.

September 30, 1939. Endometrial biopsy—late secretory phase.

October 4, 1939. Menses began and lasted five days.

Treatment was repeated after this menses and during this month the patient became pregnant. She aborted spontaneously at nine weeks' gestation. She has subsequently become pregnant again.

CASE 4

L. C., white female, age fifteen, high school student. Chief complaint—severe pain in the lower abdomen between the menses, usually occurring about half way between the menses. The menses were regular in amount and rhythm and there was no dysmenorrhea. The patient had an appendectomy for relief of one of these painful episodes with no relief. The pain was undoubtedly related to the ovulation time as the patient could foretell the time of the month when they would occur. When she was first seen she gave a history of the last menses having begun on December 2, 1939 and she was seen in acute pain on December 17, 1939.

December 27, 1939. Endometrial biopsy—marked proliferative phase.

December 30, 1939. Endometrial biopsy—marked proliferative phase.

January 1, 1940. Normal menses began.

January 7, 1940. Gonadotropic hormone 1 c.c. and this was repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

January 23, 1940. Patient stated that she suffered no pain at the mid cycle.

Endometrial biopsy—secretory phase.

January 28, 1940. Normal menses began.

February 3, 1940. Gonadotropic hormone 1 c.c. and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

February 24, 1940. No pain at the mid cycle. Endometrial biopsy—secretory phase.

Pain reappeared in March, 1940, when treatment was discontinued.

CASE 5

D. M., white female, age thirty-three, married seven years. Chief complaint—sterility. Menses always regular, normal flow without pain. Patient rather obese but otherwise in good physical condition.

May 10, 1939. Semen examination—normal in amount, normal count, motility good, and the morphology was normal under the stained smear. Huhner test with fluid from cervix and vaginal vault was positive. Pelvic examination showed a marital introitus, normal vaginal mucosa, cervix small and directed towards the symphysis, uterus in third degree retroversion but freely movable, tubes and ovaries not palpable. Rubin Test: Air passed through the tubes at 150 mm. mercury. There was a moderate erosion of the cervix which was cauterized. Endometrial biopsy (twenty-two days from the first day of the last menses)—proliferative phase.

May 18, 1939. Normal menses began.

May 24, 1939. Gonadin 1 c.c., repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

June 14, 1939. Endometrial biopsy—secretory phase.

June 17, 1939. Normal menses began.

July 14, 1939. Endometrial biopsy (no treatment in this cycle)—proliferative phase.

July 15, 1939. Normal menses began.

July 22, 1939. Gonadin 1 c.c. and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

August 21, 1939. Menses appeared and flow was normal.

August 26, 1939. Gonadin treatment was started and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

November 28, 1939. Diagnosis of pregnancy by physical examination.

CASE 6

C. I. D., white female, age twenty-six, married four years. Chief complant—sterility. Menses have been irregular since onset, sometime with periods of amenorrhea lasting three months. No other complaint. Examination revealed a healthy young woman with normally developed secondary sex char-

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acteristics. Pelvic examination showed introitus and vagina normal, cervix posterior, uterus anterior and normal size. Tubes patent at 160 mm. of mercury. B.M.R. plus 18. Semen examination—normal quantity and good motility; count 500,000,000 to the c.c.; morphology poor.

June 10, 1939. Endometrial biopsy (thirty-seven days after the last menses)—early proliferative phase—atrophic type.

June 25, 1939. Menses began and lasted three days.

June 30, 1939. Gonadin 1 c.c., and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

July 24, 1939. Endometrial biopsy—proliferative phase.

July 25, 1939. Menses began and lasted two days.

July 31, 1939. Gonadin 1 c.c., and repeated on the eighth, tenth, twelfth, thirteenth, and fourteenth day of the cycle.

September 18, 1939. Nausea and vomiting.

September 28, 1939. Diagnosis—pregnancy.

CASE 7

O. R., age seventeen, single, white. Chief complaint—primary amenorrhea. Patient has not menstruated at all. The breast development and adult hirsutism is retarded. Pelvic examination—intact hymen; by rectal examination, the internal genitalia were difficult to palpate but no gross abnormality was found. No attempt was made to obtain endometrial biopsy on account of the intact hymen.

July 1, 1939. Gonadin 1 c. c., repeated on the second, fourth, sixth, eighth, ninth, and tenth day.

July 29, 1939. Vaginal bleeding began and lasted two days with severe dysmenorrhea.

September 10, 1939. Menses appeared again, although no further treatment was given.

October 28, 1939. Menses appeared with severe dysmenorrhea.

December 18, 1939. Menses appeared and lasted three days—with no additional treatment.

NOTE: Gonadin supplied by Cutter Laboratories.

Medical Arts Building.

Correspondence

Richmond, Virginia.
October 31, 1940,

TO THE EDITOR:

Of course you have noticed the publicity Morris Fishbein gives to the fact that it will be necessary for him and some others to attend the A.M.A. trial in Washington, and the injurious effect this will have on the work of the Chicago office. He fails to mention the fact that during the ten years from 1927 to 1937 he has published thirty books or an average of three books a year. In 1937 alone he published eight books, but he has said nothing about the injurious effect such outside activities have on the work of the Chicago office.

E. C. L. MILLER, M.D.

Public Health Statistics

I. C. RIGGIN, M. D.,
State Health Commissioner of Virginia

The report of the Bureau of Communicable Diseases of the State Department of Health for October, 1940, compared with the same month in 1939, and for the period of January through October, 1940, compared with the same period in 1939, follows:

	OCT. 1940	OCT. 1939	JAN.-OCT. 1940	JAN.-OCT. 1939
Typhoid and Paratyphoid Fever	34	33	223	424
Diarrhea and Dysentery	131	167	1,716	4,055
Measles	97	23	3,458	10,755
Scarlet Fever	129	180	1,290	1,111
Diphtheria	90	296	495	1,003
Poliomyelitis	61	6	183	39
Meningitis	6	4	64	53
Undulant Fever	2	1	20	21
Rocky Mountain Spotted Fever	2	1	42	48
Tularaemia	2	5	39	56

A NEW PROGRAM FOR INDIGENT CHILDREN

The State Health Department, in cooperation with the Out-Patient Department of the Medical College of Virginia, has recently inaugurated a program for indigent children suffering from rheumatic heart disease.

There are not enough funds available to make this a state-wide program, and only patients from the city of Richmond and Henrico County are being accepted at the present time. The program will be expanded if additional federal funds are secured.

The clinic is staffed by a cardiologist, a pediatrician, a public health nurse, a social worker, and a clerk. Full diagnostic facilities are available, including routine electrocardiograms and X-rays. Hospitalization for active cases is provided in the hospital division of the Medical College of Virginia, and for convalescent cases at the Crippled Children's Hospital and Richmond Community Hospital.

A survey to determine the incidence of rheumatic fever in adolescence is being carried on at the present time. The incidence of clinical heart disease found in the survey to date is approximately one per cent. This is somewhat higher than was anticipated, but little at present is known as to the amount of rheumatic heart disease present in Virginia.

New Members

New members of the Medical Society of Virginia since the list published in the May, 1940, issue of the MONTHLY are:

Dr. Aubry C. Belcher, Richmond.
Dr. Richard Boxley Bowles, Mathews.
Dr. Ben Lynn Boynton, Norfolk.
Dr. Harry Brick, Richmond.
Dr. Leland Coffey Brown, Staunton.
Dr. John Francis Cadden, Roanoke.
Dr. Clara King Dickinson, Marion.
Dr. Thomas Southgate Ely, Middlesboro, Ky.
Dr. Sandidge Evans, McClure.
Dr. David Samuel Garner, Roanoke.
Dr. Harold Marshall Goodman, Richmond.
Dr. Marvin Swindell Herrington, Norfolk.
Dr. Cecil William Hickam, Pulaski.
Dr. Chester Frederick Hogan, Richlands.
Dr. Harry Wynn Hollingsworth, Derby.
Dr. Horace Dunbar Hoskins, Lynchburg.
Dr. Edwin Lawrence Kendig, Jr., Richmond.
Dr. Beverley Randolph Kennon, III, Norfolk.
Dr. Jefferson Bishop Kiser, Emporia.
Dr. George McLean Lawson, Charlottesville.
Dr. Robert Bruce Mallett, Orange.
Dr. Joseph Lee Mann, Hampton.
Dr. Theodore Baldwin McCord, Fairfax.
Dr. Lewis Alan Micou, Eagle Rock.
Dr. Lyddane Miller, Piney River.
Dr. Edward Albert Mitchell, Clinchco.
Dr. Francis Newby Mullen, Jr., Norfolk.
Dr. Samuel Morton Novak, Alexandria.
Dr. Joseph Thomas Phillips, Jr., Norfolk.
Dr. Marion Timothy Plyler, Jr., Whaleyville.
Dr. Samuel Byron Pope, Jr., Norfolk.
Dr. Walter John Rein, Richmond.
Dr. Irwin Rifkin, Richmond.
Dr. Carter Reed Rowe, Fredericksburg.
Dr. Edwin Macrae Rucker, Richmond.
Dr. Leo Solet, Arlington.
Dr. Alexander Armstrong St. Clair, Richlands.
Dr. Thomas Sydney Ussery, Norton.
Dr. Richard Wingfield Vaughan, Richmond.
Dr. Thomas Duval Watts, Richmond.
Dr. George A. Welchons, Brook Hill.
Dr. Samuel Harrison Williams, Alexandria.
Dr. Washington Carlyle Winn, Richmond.

Woman's Auxiliary to the Medical Society of Virginia

President—MRS. GRIFFIN HOLLAND, Eastville.
President-Elect—MRS. E. LATANE FLANAGAN, Richmond.
Recording Secretary—MRS. HAROLD W. POTTER, Hilton Village.
Corresponding Secretary—MRS. J. WALKER JACKSON, Machipongo.
Parliamentarian—MRS. JAMES B. STONE, Richmond.
Treasurer—MRS. REUBEN F. SIMMS, Richmond.
Chairman, Press and Publicity—MRS. HENRY M. SNEAD, Petersburg.

Norfolk Auxiliary.

The Woman's Auxiliary to the Norfolk County Medical Society held its first fall general meeting on November 4, with the new president, Mrs. A. G. Horton, presiding.

Plans for the year were outlined. The Public Relations chairman announced that the Auxiliary would work with the Red Cross headquarters one day each month as a part of their program. The sale of *Hygeia* was discussed and arrangements made for several gift subscriptions to public institutions. Layettes are again being made for poor families and much interest is shown in doing this.

News from the *Bulletin of the Auxiliary to the American Medical Association* was reviewed by one of the members and it is hoped that much information and inspiration may be received from these Bulletin reviews at each meeting.

The younger members of the Auxiliary are taking a most active and interested part in Auxiliary work which is a sure sign of a wide-awake organization and which is most gratifying to the officers and older members.

R. WILSON,
Publicity Chairman.

SUBSCRIBE TO THE BULLETIN—

The official publication of the Woman's Auxiliary to the American Medical Association, issued quarterly, $1.00 a year. Send subscriptions to Mrs. H. E. Christenberry, Highland Drive, Knoxville, Tenn., or to the State Chairman, Mrs. E. Holland Trower, Eastville, Va.

Book Announcements

Medical Work of the Knights Hospitaliers of Saint John of Jerusalem. By EDGAR ERSKINE HUME, Lieutenant-Colonel, Medical Corps, United States Army, Knight of Honor and Devotion of the Sovereign Military Order of Malta. Foreword by His Most Eminent Highness Fra Ludovico Chigi-Albani, Prince Grand Master of the Sovereign Military Order of Malta. Preface by Lieutenant-General Sir Aldo Castellani, K.C.M.G., Count of Chisimaio, Magistrat Knight of the Sovereign Military Order of Malta, Professor at the Universities of Rome, London and Louisiana. Baltimore. The John Hopkins Press. 1940. xxii-371 pages. Illustrated. Cloth. Price, $3.00.

Reviewed editorially in this issue.

The Practice of Medicine. By JONATHAN CAMPBELL MEAKINS, M.D., LL.D., Professor of Medicine and Director of the Department of Medicine, McGill University; Physician-in-Chief, Royal Victoria Hospital, Montreal; Formerly Professor of Therapeutics and Clinical Medicine, University of Edinburgh; etc. Third Edition. St. Louis. The C. V. Mosby Company. 1940. Octavo of xvi-1430 pages. With 562 Illustrations Including 48 in Color. Cloth. Price, $10.00.

Reviewed editorially in this issue.

Diagnosis and Treatment of Diseases of the Hair. By LEE McCARTHY, M.D., Member of the American Dermatological Society; Attending Dermatologist to Garfield Memorial Hospital; Consulting Dermatologist to the U. S. Naval Hospital; etc. St. Louis. The C. V. Mosby Company. 1940. Octavo of 671 pages. With 291 Illustrations Including 7 in Color. Cloth. Price, $9.50.

The following remarks are made by the author in the preface. "Many physicians, and not a few dermatologists, profess an almost complete ignorance of the cause of many diseases of the hair, and they are accordingly unable to answer questions put to them by their patients. As a result, the coiffeurs and beauticians are consulted today much more frequently on this subject than are physicians. * * * We should all be able to tell our patients what types of treatment are worthless, even though we cannot cure all the ills of the hirsute system."

There have been very few books in the English language devoted to diseases of the hair, and the author of this one is particularly well qualified to write this volume, because he has been a student of Sabouraud. Sabouraud probably was the greatest modern trichologist.

This work is very well done and complete. Of particular merit are the sections on alopecia areata, fungus infections of the hair, and seborrhea. The author has devoted some space to the historical aspect of alopecia areata and tineas of the scalp. The description of Fox-Fordyce Disease is good.

The author and the publisher are to be congratulated on this excellent volume.

ALLEN PEPPLE, M.D.

Compendium of Regional Diagnosis in Lesions of the Brain and Spinal Cord. A Concise Introduction to the Principles of Localization of Diseases and Injuries of the Nervous System. By ROBERT BING, Professor of Neurology, University of Basel, Switzerland. Translated and edited by WEBB HAYMAKER, Assistant Clinical Professor of Neurology and Lecturer in Neuro-Anatomy, University of California. Eleventh Edition. St. Louis. The C. V. Mosby Company. Octavo of 292 pages. Illustrated. Cloth. Price, $5.00.

This brief but thorough book concerning the anatomy and regional localization of lesions in the nervous system has remained popular for thirty years, and the eleventh edition is thoroughly up-to-date.

It is almost impossible to avail one's self of good anatomic description and illustration, accompanying logical physiologic and pathologic data covering the brain and spinal cord in such compact easily readable and understandable fashion. Such a book with 125 illustrations, many in color, should be available to all medical students and physicians interested in the field of neurology. J. L. THOMSON.

The 1940 Year Book of Public Health. Edited by J. C. GEIGER, M.D., Dr.P.H., Director of Public Health, City and County of San Francisco; Clinical Professor of Epidemiology, University of California. The Year Book Publishers, Inc. Chicago, 1940. 560 pages. Cloth. Price, $3.00.

This Year Book is really a series of abstracts of many articles in the public health field published over the last year or two. The subjects covered are communicable diseases, epidemiology, food and milk, nutrition, housing, statistics, laboratory and industrial hygiene, administration which includes administration of medical and maternal care as well as public health, health education and child hygiene. Under the latter is included dental hygiene, mental hygiene and nursing.

Articles on all the important communicable diseases published during the last year have been abstracted. The other subjects outlined above are covered in the same way and the volume gives a good review on work that is being done in these different fields. If anyone wants to go into any subject more thoroughly, he can do that by referring to the original articles. The book will be of much value to the health officer, the epidemiologist, and the laboratory worker. FRED J. WAMPLER, M.D.

Virginia Medical Monthly

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Editorial

The Theory of Diabetes.

In diabetes, is a pathological pancreas *the* cause, or is functional deficiency of the islands of Langerhans merely relative to something else? This is the point on which the thought of theorists and the work of experimentalists has centered for a long time. After the introduction of insulin the pure pancreatists held the field for a while, almost undisputed. Then, recovering somewhat, the skeptics began to accumulate new evidence to the effect that overactivity of the anterior pituitary and, by inference at least, overactivity of the adrenal cortex, and impairment of liver function, each, has an influence on carbohydrate metabolism which may be primarily responsible for the diabetic state, directly or through an effect on the pancreas. Then there is the experience in the clinic of lessened intensity of diabetes after thyroidectomy in exophthalmic goiter. Altogether, the champions of extra-pancreatic factors, like Mrs. Browning in her *Aurora Leigh*, have charged that, verily, many thinkers of this age understand the subject "too insularly".

The clinician has a deep interest in all this. It was through the work of men concerned with advanced aspects of the subject that the clinician was taught something about the relationship between carbohydrate and fat metabolism and the prevention of ketosis. But in the great majority of cases the clinician, armed with insulin, may for the present hold to the insular viewpoint. Not until they had carefully weighed the newer data did Warren and Wilder give expression to these two guiding principles:

Said Warren: So much experimental evidence ties the pituitary to diabetes that we are prone to forget that nature herself gives us but few examples of diabetes associated with pituitary change, and those are of a distinctive form.

And Wilder: It seems to me that we still ought to adhere to the theory of diabetes as it originally was maintained by Naunyn that with very rare exceptions the primary cause is an inborn biologic inferiority, primarily of the insular reserve.

This thesis, Wilder said, is accepted by many authorities, including Umber, Joslin—with some reservation—and Woodyatt.

J. H. SMITH.

Comments on Crockett's Revision.

In this issue there is presented the first revision of the list of commercial preparations of hormones originally published in this JOURNAL (66:191, 1939) by the late Professor W. G. Crockett. The wide demand for reprints of Dr. Crockett's first article, by physicians, pharmacists and pharmaceutical firms, is proof of the importance of his summary. On the day of his death he sent me this paper for final criticism. Except for some minor changes it remains essentially as he wrote it.

Probably the most important advance, noticeable in this revision, is the increase in the number and variety of estrogenic preparations. Unfortunately, there is much confusion existing among practitioners concerning the relative efficiency of these substances, as estradiol, estradiol benzoate or di-propionate, estrone, and estriol. Both estrone and estriol may be rated in international units (I. U.)—one unit representing the activity of 0.1 gamma (1/10,000 mg.) of pure estrone, as tested usually by the vaginal smear method in castrated female rats.

However, since the benzoate ester of estradiol has a much longer lasting effect, even when the *intensity* of response is the same as estrone, an international estradiol benzoate unit has been established. The end result of having two such units, however, is confusing. Since most of the commercial products are now in pure form, some synthesized from others, in my opinion it is advisable to disregard international units entirely, and to prescribe dosages in milligrams.

Of course, a milligram of estradiol is much more effective (about 12 times) than one of estrone. However, since I know of no work proving any essential difference in the physiologic effects of the various estrogens, I believe it best for a physician to select one preparation and use it constantly, rather than use several and thereby be constantly concerned about how much of one is equivalent to so much of another. Few men in general practice would consider using leaf digitalis on one patient, ouabain on another, and a pure glycoside on a third, nor would they shift indiscriminately from one brand of dried thyroid to another. Why should we not look upon the estrogens in the same way?

One notes that some of the estrogenic preparations in Dr. Crockett's list, are designated only by their proprietary name, and no statement is made concerning which estrogenic hormone they contain. This is due to the fact these concerns do not give this information in their literature, either because they do not know—or as I have been told—that a question of patent rights is involved. If the latter is true, then it is truly regrettable that such legal technicalities should be permitted to interfere thus with full and correct labeling of a drug. However, I feel sure that all such undescribed preparations, when dissolved in oil at least, may be considered to be estrone.

There are a few practical points that may be well kept in mind concerning the administration of estrogen:

1. Oral administration of an estrogen requires perhaps eight or ten times as much as is administered intramuscularly. This is probably because of the fact that the liver detoxifies the hormone as it is absorbed from the gut.

2. The esters of estradiol, as the benzoate and di-propionate, have a longer lasting effect than estradiol, probably due to slower absorption. Perhaps they may be better suited for intramuscular administration because of this fact. However, some authors believe that it may be inadvisable to inject the foreign-oil vehicles of these preparations over long periods of time, because of local reactions.

3. Patients will differ remarkably in the dosage needed. For instance, one patient may complain of severe mastodynia from moderate doses of estradiol benzoate, whereas another may take twice as much without such symptoms. Of course, due to the cost of the products, the menopausal patient should determine herself what is the minimal amount she needs for relief of her condition.

4. For oral administration, water-soluble estriol is probably preferable to lipoid-soluble estrone, and free alpha-estradiol is preferable to its more insoluble esters.

5. The use of estrogenic hormones may be contraindicated in early pregnancy.

It is of interest that a recent assay by Goldman and Cinberg (Endoc. *27*:524, 1940) of the potency of five commercial preparations of pituitary gonadotropin has shown them to be far below their stated strength, due probably to deterioration.

R. J. MAIN.

Paging Dr. Doe (to ask if he has filled out his questionnaire).

To every doctor in the State of Virginia, as to doctors in every other state in the Union, a question-

naire was recently sent by the American Medical Association. By means of the facts contained in the answers to the questionnaire the members of the medical profession will be assorted as to age, qualifications, disability and preference of service. The information will be handed over to the War Department in Washington and on the basis of it the medical department of the Army and Navy will be organized for war. The importance of the proper filling out and the prompt returning of the questionnaire by every doctor, irrespective of his age or any disability, is obvious. The doctors of Virginia who have not yet performed this duty are again urged to do so. It might interest those doctors within the age limit of the draft to know that they are subject to the draft, and, unless registered in Washington by the A.M.A. through their properly answered questionnaires, they may be called into the service in departments other than those in which they should be able to do most for their country because of their training.

Jonathan Meakins's Third.

Is it audacious for one man to attempt unaided to write a treatise on the practice of medicine at a time when specialization is so much to the fore? Meakins does not think so. Sir William Osler did not think so. Nor do many others who feel that the unity of a presentation has a value of itself, that the balance, the varying emphases placed upon the component parts of the whole, and the method of correlation into a whole are of themselves important in giving an understanding of the whole.

Meakins, in the third edition of his *Practice of Medicine,* has produced single-handed a serviceable text with a profusion of excellent illustrations. His emphasis is upon the fact that from a patient's existing symptoms and signs, which indicate disturbance of functions, pathological changes may be traced and identified. To symptoms as the first and earliest sign of disease he gives particular prominence. This is as it should be. He takes account of rapid changes in medical knowledge, such as, for instance, the chemotherapy of pneumonia, the part of Vitamin K in hemorrhagic disease associated with liver pathology, sarcoidosis as a general disease, the newer knowledge regarding hypertension, and the newest conceptions of the role of the liver in circulatory failure.

Among the present generation of medical books, Meakins's ranks high. Students and practitioners are fortunate if they have a copy on hand for ready reference.

The Knights of St. John.

Those who have heard Colonel Edgar Erskine Hume lecture on the medical work of the Knights Hospitallers of St. John of Jerusalem, have hoped that he would put his material into book form. That wish has now been fulfilled. The Johns Hopkins Press has recently issued a book attractively printed and richly illustrated to make permanent the results of this piece of research.

It is interesting to know that this is the first comprehensive account in English of the medical work of a remarkable order which has existed since the Eleventh Century. Of the Knights' deeds and bravery on land and sea much has been written, but little of their humanitarian service in Rhodes and Malta and throughout war-torn countries during many centuries has been told until now.

Colonel Hume's account is a fascinating story of the accomplishments of this Sovereign Military Order of Malta.

Subjugation of Tuberculosis.

"One of the great achievements of the 20th century will be the subjugation of tuberculosis", said Henry D. Chadwick in his presidential address before the National Tuberculosis Association at Cleveland.

Delegates were reminded, however, that before the goal can be reached, certain wide gaps in the program of research, case-finding and provision of treatment facilities, must be closed. There is as yet no specific cure, no dependable vaccine; chemotherapy offers scant encouragement, case-finding is still too haphazard and at least 60,000 more beds for tuberculous patients are needed.

The need for additional beds is evident when we face the fact that those states which have provided the minimum of two beds for each annual death have reduced their death-rate much more rapidly than those with one bed. Fourteen states have failed to provide even one bed and the majority of them are in the South. The death-rate in thirteen of these states exceeds the average for the country as a whole.

It is interesting as well as challenging to note the death-rate for Virginia as compared with the average for the nation. In 1939 the rate for the nation was 46.5 per 100,000 population and 66.2 for the State of Virginia.

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Additional beds for the tuberculous placed where most needed should be the No. 1 item on the agenda of the tuberculosis campaign. Health Education as it applies to tuberculosis seems to be item No. 2. It is in the latter field that individual contributions to the voluntary tuberculosis associations through the purchase of Christmas Seals will be most effective. These organizations furnish information to the individual, to the community and to the governing bodies in the various localities, which results in increased appropriations for sanatoria care, clinic service, collapse therapy and above all, an enlightened public. Each year, hundreds and hundreds of Virginians seek medical aid while the disease is still in the early stages. We should see to it that their hopes for help are not disappointed.

A. B. C.

Department of Clinical and Medical Education of the Medical Society of Virginia

Postgraduate Clinic.

The twenty-sixth postgraduate clinic was held at the University of Virginia on November 8 and 9. It consisted of a Symposium on Obstetrics and Gynecology conducted by eminent specialists in the field. The full program was printed in the November issue of the VIRGINIA MEDICAL MONTHLY. Following the afternoon program on Friday the visitors were entertained at dinner by the Department of Obstetrics and Gynecology at the Farmington Country Club. Dr. and Mrs. Tiffany Williams entertained for them at their home following the James Carroll Flippin lecture on Friday evening.

The following doctors registered for the clinic:

Dr. L. M. Allen, Winchester.
Dr. H. L. Baptist, Ivy.
Dr. Joseph Bear, Richmond.
Dr. H. G. Bland, Newport News.
Dr. R. E. Booker, Lottsburg.
Dr. G. S. Bowers, Frostburg.
Dr. John O. Boyd, Roanoke.
Dr. James G. Brown, Woodville.
Dr. W. E. Brown, Blue Ridge Sanatorium.
Dr. E. W. Buckingham, Newport News.
Dr. A. C. Byers, Harrisonburg.
Dr. F. L. Byers, Harrisonburg.
Dr. H. G. Byrd, Louisa.
Dr. G. C. Campbell, Staunton.
Dr. B. L. Carleton, Newport News.
Dr. A. L. Carson, Jr., Richmond.
Dr. H. T. Chelf, Culpeper.
Dr. J. C. Coulter, Charlottesville.
Dr. Frank Daniel, Charlottesville.
Dr. H. S. Daniel, Louisa.
Dr. A. C. Davis, Roanoke.
Dr. E. D. Davis, Crozet.
Dr. C. O. Dearmont, White Post.
Dr. H. T. Dickie, Roseland.
Dr. C. W. Dorsey, Roanoke.
Dr. E. B. Dovell, Unionville.
Dr. L. C. Downing, Roanoke.
Dr. Elizabeth Edmunds, Lynchburg.
Dr. E. M. Ellerson, Staunton.
Dr. E. E. Epperson, Meadow View.
Dr. C. F. Gaylord, Staunton.
Dr. G. G. Gooch, Roanoke.
Dr. A. M. Groseclose, Roanoke.
Dr. E. S. Groseclose, Lynchburg.
Dr. A. B. Grubb, Cripple Creek.
Dr. J. M. Habel, Suffolk.
Dr. Percy Harris, Scottsville.
Dr. W. F. Hartman, Swoope.
Dr. H. H. Hazen (Speaker), Washington, D. C.
Dr. M. B. Hiden, Leesburg.
Dr. R. W. Holmes, Chicago and Charlottesville.
Dr. George Hurt, Roanoke.
Dr. J. Paul Kent, Alta Vista.
Dr. E. C. Kidd, Lovingston.
Dr. D. M. Kipps, Front Royal.
Dr. W. A. Kyger, Free Union.
Dr. Henry J. Langston, Danville.
Dr. T. C. Lawford, Newport News.
Dr. Charles E. Llewellyn, Richmond.
Dr. Anita Lotti, Charlottesville.
Dr. J. F. McGavock, Crozet.
Dr. C. E. McLennan, Minneapolis, Minn.
Dr. Margaret McLennan, Minneapolis, Minn.
Dr. R. H. Manson, McKenney.
Dr. T. A. Moneymaker, Washington, D. C.
Dr. R. Morgan, Roanoke.
Dr. N. P. Moss, Roanoke.
Dr. J. O. Mundy, Charlottesville.
Dr. R. D. Mussey (Speaker), Rochester, Minn.
Dr. Dan O. Nichols, Charlottesville.
Dr. S. E. Oglesby, Lynchburg.
Dr. W. H. Paine, Charlottesville.
Dr. T. E. Patteson, Ransons.

Dr. Harrison Picot, Alexandria.
Dr. F. O. Plunkett, Lynchburg.
Dr. B. F. Randolph, Arrington.
Dr. C. M. Rice, Sweet Briar.
Dr. C. L. Riley, Winchester.
Dr. L. G. Roberts, Moorman's River.
Dr. M. P. Rucker (Speaker), Richmond.
Dr. J. R. Saunders, Madison Heights.
Dr. E. C. Schelin, Richmond.
Dr. S. W. Selden, Kents Store.
Dr. L. L. Shamburger, Richmond.
Dr. J. A. Sims, Alexandria.
Dr. H. C. Spaulding, Richmond.
Dr. H. J. Steele, Bluefield, W. Va.
Dr. E. W. Stratton, Charlottesville.
Dr. W. D. Suggs, Richmond.
Dr. J. F. Thaxton, Tye River.
Dr. J. A. M. Thompson, Blue Ridge Sanatorium.
Dr. N. A. Thompson, Danville.
Dr. P. E. Thornhill, Norfolk.
Dr. H. F. Traut (Speaker), New York City.
Dr. H. H. Ware, Jr., Richmond.
Dr. A. D. F. White, Lynchburg.
Dr. J. M. Whitfield, Richmond.
Dr. M. H. Winer, Charlottesville.
Dr. W. C. Winn, Richmond.
Dr. William H. Wood, Jr., Charlottesville.
Dr. F. H. Yorkoff, Clintwood.

Local Courses.

Dr. Hugh H. Trout, retiring President of the Medical Society of Virginia and the new Chairman of this Department, recently sent letters to each component society offering the assistance of the Department in arranging programs and providing speakers on local clinics. Societies wishing to take advantage of this offer of assistance should communicate with the Executive Secretary.

GEORGE B. ZEHMER,
Executive Secretary.

Proceedings of Societies

Louisa County Medical Society.

At a called meeting of this Society in Mineral, on October 28, the following officers were elected: President, Dr. H. G. Byrd, Louisa; and secretary-treasurer, Dr. E. B. Pendleton, Cuckoo.

A county-wide small-pox vaccination program for school children was adopted for the near future, and the society agreed to aid the county school teachers in their annual health inspection.

The Dickenson-Buchanan County Medical Society

Met at Grundy Hospital, Grundy, on October 23, Dr. J. C. Moore, President, of Keen Mountain, presiding. A committee on Medical Preparedness was appointed as follows: Dr. A. S. Richardson, chairman, Dr. J. C. Trivett, Dr. D. F. Love, Dr. E. M. Fusco, and Dr. George Snead. Dr. H. M. Kelso, Abingdon, and Dr. C. W. Scott, of State Health Department, gave an interesting talk on the Tuberculosis Situation in Southwestern Virginia. The principal address was by Dr. A. L. Carson, Jr., of the State Health Department, on Syphilis in Pregnancy.

This society meets monthly, with an average attendance of about twenty members. Dr. T. C. Sutherland, Haysi, is secretary-treasurer.

The Tazewell County Medical Society

Met on November 14 in Tazewell. Dr. F. H. Smith, Abingdon, was the speaker, his topic being "The Sulfanilamide Group in the Service of the General Practitioner". The following were elected to membership: Dr. J. W. Houck, Dr. G. D. Vermilya, and Dr. Lee Harris, all of Richlands.

Dr. J. P. Williams, Richlands, is president of this society and Dr. Mary Elizabeth Johnston, Tazewell, is secretary.

Augusta County Medical Association.

This Association held its quarterly meeting early in November at the Stonewall Hotel in Staunton, at which time Dr. Samuel A. Vest of the University of Virginia gave a talk on "The Male Hormone", and Dr. Kenneth Bradford of Staunton gave an illustrated case report on "The Treatment of Spontaneous Pneumothorax". Dinner followed. Dr. S. H. Garst of Staunton is president and Dr. J. E. Cox of Waynesboro secretary of the Association.

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Lynchburg Academy of Medicine.

At the regular meeting on September 9, Dr. Walter B. Martin, Norfolk, spoke on his experimental work using sulfapyridine and sulfathiozol in the treatment of staphylococcus infections. His lecture was illustrated with many spectacular cases of recovery.

Dr. George S. Bowers, Rustburg, was elected to membership.

It was decided that members in good standing who are called to active service as a result of the defense program should retain their full membership and be relieved of payment of dues while in the service.

Resolutions on the death of Dr. James Morrison were presented from the Junior Journal Club of Lynchburg, of which Dr. Morrison was an original member.

Dr. R. Finley Gayle, Jr., Richmond, gave an illustrated lecture on "The Treatment of Parkinsonism with Belladonna Alkaloids", at the October meeting.

The Society tabled indefinitely any action on equalizing medical cost to men serving in the emergency program. The committee on National Preparedness was appointed as follows: chairman, Dr. R. D. Caldwell, Dr. D. M. Thomasson, Dr. James Gorman, Dr. Bernard Kyle, and Dr. Edwin Harper, with Drs. George Tompkins, Powell Dillard and H. P. Brown, as alternates.

The November meeting was held on the 4th and the entire program was devoted to fractures. Dr. H. H. Wescott, Roanoke, presented a paper on "First Aid Treatment of Fractures", and Dr. O. L. Miller, Charlotte, N. C., an illustrated paper on "Trauma In and Near the Hip Joint". Both papers were generally discussed.

Dr. E. G. Scott is president of the Academy and Dr. C. E. Keefer, secretary-treasurer.

News Notes

The Southern Medical Association

Had an attendance of over 2,500 at its meeting in Louisville, November 13-15, more than two thousand of whom were physicians. Virginia had a representation of about sixty, many of whom were accompanied by their wives. The President-elect, Dr. Quitman U. Newell of St. Louis, having died on the 4th of November, Dr. Paul H. Ringer of Asheville, N. C., was elected president to succeed Dr. Arthur T. McCormack. Other officers are: President-elect, Dr. M. Pinson Neal, Columbia, Mo.; vice-presidents, Dr. E. Lee Heflin of Louisville and Dr. James R. Bloss of Huntington, W. Va. Mr. C. P. Loranz continues as Secretary-Manager, and Dr. M. Y. Dabney as editor of the Journal. The next meeting of the Association will be held in St. Louis, Mo., in November, 1941.

Virginia doctors noted as officers in sections are: Dr. Austin I. Dodson of Richmond as secretary of the Section on Urology; Dr. David C. Wilson of Charlottesville as chairman of the Section on Neurology and Psychiatry and Dr. Harvey B. Haag of Richmond as chairman of the Medical Education Section.

The Seaboard Medical Association of Virginia and North Carolina

Is meeting in Washington, N. C., December 3 to 5, under the presidency of Dr. John Cotten Tayloe of that place. An interesting program includes papers by a number of members and guests.

Married.

Dr. Hubert Dinwiddie Crow, Lawrenceville, and Miss Pattie Gregg Featherstun, Richmond, November 18. Dr. Crow is a graduate of the Medical College of Virginia, class of '38.

Dr. Homer Jackson Hancock, Welch, W. Va., and Miss Harriet Loyd Hudgins, Warrenton, N. C., October 26. Dr. Hancock graduated from the Medical College of Virginia in 1937, and is at present connected with the staff of the Stevens Clinic Hospital at Welch.

Dr. Francis Nicholson Taylor and Miss Sarah Elizabeth Madison, both of Petersburg, November 12.

News from Medical College of Virginia.

Dedication of the new teaching hospital at the Medical College of Virginia, Richmond, will

take place on Founders' Day of the institution, Thursday, December 5, twelve o'clock noon. Among those participating will be Governor James H. Price; Colonel E. W. Clark, Public Works Administration; Dr. Walter L. Bierring, past president, American Medical Association; Dr. Walter B. Martin, president, Medical Society of Virginia; Dr. H. E. Jordan, Dean, Department of Medicine, University of Virginia; Mr. M. Haskins Coleman, Jr., Secretary, Richmond Hospital Council, and Dr. Lewis E. Jarrett, Director of the Hospital Division, Medical College of Virginia. A notable group of visitors is expected. Beginning at two o'clock in the afternoon the new hospital will be open for inspection to the general public, and on Tuesday night, December 3, a reception and hospital open house will be observed at the new hospital for the local medical profession and specially invited guests.

The new hospital, completed at a cost of approximately $2,500,000.00, with equipment, provides for two new services here, neuropsychiatry and contagious diseases, enlarged facilities for physical therapy and many other activities including ample provision for teaching.

Dr. Walter L. Bierring, President, and Dr. J. J. Moore, Secretary, of the Alpha Omega Alpha national honorary medical fraternity, will participate in the installation of a chapter of this fraternity at the Medical College of Virginia on Wednesday, December 4.

News from University of Virginia.

On October 10, Dr. Andrew D. Hart, Jr., spoke before the Alexandria Medical Society, meeting in Alexandria, on the subject, Psychosomatic Medicine.

Dr. T. J. Williams addressed the Peninsula Academy of Medicine, meeting at Old Point Comfort, on October 21. His subject was Ovarian Hormones in Obstetrics and Gynecology.

On October 22, The Faculty of the Department of Medicine gave a dinner in honor of Mr. John J. Moran of Habana, Cuba. After the dinner General Jefferson R. Kean, U. S. A., Retired, gave an account of Dr. Walter Reed's experiences as Director of the Commission sent to Cuba in the summer of 1900 to study the cause and prevention of yellow fever and Mr. Moran's contribution to this study was one of the experimental subjects inoculated with the yellow fever virus by the bite of a mosquito.

Dr. Fletcher D. Woodward addressed the Tennessee Valley Medical Assembly in Knoxville, on October 10 and 11. His subjects were The Value of Bronchoscopy and Esophagoscopy in the Diagnosis of Obscure Chest Conditions and The Result of Treatment of Certain Malignancies about the Larynx, Throat and Sinuses.

The University has announced a new scholarship in the Department of Medicine. This scholarship was founded in 1939 upon the bequest of Dr. James L. Minor, a distinguished Ophthalmologist of Memphis, Tennessee. It carries an annual stipend of $350.00.

At the fall meeting of the Northern Neck Medical Association held in Stratford, on October 24, Dr. H. B. Mulholland spoke on The Treatment of Pneumonia, Dr. A. D. Hart, Jr. discussed Psychosomatic Medicine and Dr. Byrd S. Leavell spoke on The Anemias.

On October 28, Dr. Staige D. Blackford presented a paper on The Pathogenesis of Spontaneous Pneumothorax with Illustrative Cases before the American Clinical and Climatological Association, meeting in White Sulphur Springs, W. Va.

On November 6, Dr. Samuel A. Vest addressed the Augusta County Medical Society, meeting in Staunton, on the subject, Male Hormones.

Dr. J. M. Meredith attended the twenty-first annual meeting of the Association of Surgeons of the Chesapeake & Ohio Railway on November 8 at White Sulphur Springs, W. Va., and discussed a paper given by Dr. C. C. Coleman of Richmond.

The twenty-sixth Postgraduate Clinic sponsored by the University Medical School and the Division of Extension was held on November 8 and 9 with the program arranged as a Symposium on Obstetrics and Gynecology. On Friday, Dr. H. H. Hazen, Consultant Dermatologist to the United States Public Health Service, discussed Syphilis in Pregnancy; Dr. James R. McCord, Professor of Obstetrics and Gynecology at Emory University, spoke on Puerperal Infections; Dr. Herbert F. Traut, Associate Professor of Obstetrics and Gynecology at Cornell University, spoke on Pyelitis in Pregnancy; Dr. Maurice B. Strauss, of Boston City Hospital, discussed Anemias of Pregnancy; and Dr. M. Pierce Rucker, of Johnston-Willis Hospital, Richmond,

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spoke on Maternal Health in Virginia. On Friday evening, Dr. Robert D. Mussey, of the Mayo Clinic, gave the James Carroll Flippin Lecture, speaking on The Toxemias of Pregnancy. On Saturday, Dr. David A. Cooper, Assistant Professor of Medicine at the University of Pennsylvania, discussed Tuberculosis in Pregnancy; Dr. Edwin C. Hamblen, Associate Professor of Obstetrics and Gynecology at Duke University, spoke on Endocrine Therapy of Ovarian Failure during Reproductive Period; and Dr. Clarence J. Gamble, of Milton, Massachusetts, discussed Planned Parenthood and presented a film on The Technique of Contraception. Ninety-two physicians registered for the Clinic.

During the meetings of the Southern Medical Association in Louisville, on November 11, Dr. Vincent Archer, Chairman of the Council, gave a radio address of eight minutes, speaking on the subject of X-rays in Present Day Medicine. During the meetings he also addressed the Woman's Auxiliary and discussed Dr. Edwin Ernst's paper on The Roentgen Examination of the Mandibular Joint.

At the same meeting Dr. Glassell S. Fitz-Hugh presented a paper on Tracheotomy—An Analysis of a Series of 100 Consecutive Cases.

At the meeting of the University of Virginia Medical Society on November 11, Dr. Thomas J. Kirwin, of New York Hospital, spoke on the subject of Bladder Tumors.

The Neuropsychiatric Society of Virginia

Met at the University of Virginia on October 16 and the following program was presented: The Effect of Metrazol on Living Nerves by Dr. C. C. Speidel; The Relationship of the Emotions to the Hypothalamus by Dr. Beverley R. Tucker of Richmond; A New Syndrome of Vascular Headache: Results of Treatment with Histamine by Dr. Bayard T. Horton of the Mayo Clinic; The Localization of a Focus by Means of an Electroencephalogram by Dr. C. G. Holland; The Mental Hygiene of Reading Disability by Dr. Robert Stone of Marlboro, New Jersey; and Clinical-Pathological Conference by Drs. J. M. Meredith, D. C. Wilson and C. G. Holland. There were seventy-five physicians in attendance.

Dr. Alfred W. Norris,

Class of '37, Medical College of Virginia, has moved from Jonesport, Maine, and is now located in Benson, N. C.

Dr. W. S. Burton,

Formerly of Powhatan, is now connected with the Division of Venereal Disease Control of the State Health Department with offices at Long Branch, East Hampton.

Psychiatrists Organize for Public Education Work.

The Committee on Public Education of the American Psychiatric Association has announced an organization of twelve regional districts, each headed by a nationally known psychiatrist, to cooperate with the press and otherwise to foster the dissemination of sound psychiatric information to the public. Dr. Winfred Overholser, superintendent of St. Elizabeth's Hospital, Washington, is regional chairman for this district.

One of the principal aims will be to accquaint the public with the fact that a well-staffed, well-equipped hospital for the care of the mentally ill is not a luxury, but a basic necessity in any civilized community.

Dr. D. Hunter Marrow,

After a summer spent at his home in Boydton, has left for Florida and will be at Daytona Beach for the winter months.

Personnel Notes from State Health Department.

The appointment of Dr. Henry G. Steinmetz as Health Officer of Pulaski County has been cancelled and he will remain in Arlington County as Assistant Health Officer.

Dr. J. C. Neale, Jr., Assistant Director of Rural Health for the Southeast Health District, has now moved into his permanent office in Essex Building in Norfolk.

Dr. Allen W. Lane, recently Assistant Health Officer in Brunswick - Greensville - Mecklenburg Health District, has just entered upon his new duties as Health Officer of Pulaski County, with headquarters in Pulaski.

Dr. Hubert D. Crow, formerly of Buckingham, has succeeded Dr. Lane as Assistant Health Officer, in the above counties, with headquarters at Lawrenceville.

Dr. J. Gordon Rennie,

Recently of Bedford, announces his association with the Pulaski Hospital at Pulaski, and with Dr. D. S. Divers and Dr. C. W. Hickam in the practice of surgery.

Virginia Cancer Foundation.

At its recent meeting in Charlottesville, Dr. J. Shelton Horsley, Sr., of Richmond, was elected president of the Foundation, which is affiliated with the American Society for the Control of Cancer. Dr. E. P. Lehman of the University of Virginia, a director for the National organization, was re-elected a director of the Virginia Foundation, and Dr. W. D. Haden of Charlottesville will be treasurer.

American Clinical and Climatological Association.

At the meeting of this Association at White Sulphur Springs, W. Va., this Fall, Dr. William H. Higgins of Richmond was elected a member. This is considered an honor as the membership is limited. Other Virginia members are: Drs. Staige D. Blackford, H. B. Mulholland and J. Edwin Wood of Charlottesville, and Drs. James P. Baker, Wyndham B. Blanton, James H. Smith and William B. Porter of Richmond, the last named being the retiring president.

Dr. C. C. Coleman

Of Richmond conducted a panel discussion on Penetrating Wounds of the Brain, at the Clinical Congress, American College of Surgeons, recently held in Chicago. His collaborators were Dr. Howard Naffziger of San Francisco and Dr. Wallace D. Hamby of Buffalo.

The Mental Hygiene Society of Virginia,

Meeting in Richmond, October 31, was well attended and the sessions were both interesting and instructive. The speakers were Dr. Joseph E. Barrett, clinical director, Southwestern State Hospital, Marion, who presented "Some Comments on Problems of the Adolescent"; Dr. Frank Curran, senior psychiatrist, Bellevue Hospital, New York City, whose subject was "Treatment of Juvenile Delinquency at Bellevue Hospital"; and Dr. Lawrence Kolb, Assistant Surgeon General, U. S. Public Health Service, Washington, D. C., who spoke on "Mental Health and National Defense". Dr. Rowland Egger, director of the State Budget, also gave a talk entitled "A Public Administrator Looks at Mental Hygiene".

Dr. David C. Wilson of Charlottesville was elected president, succeeding Dr. O. B. Darden of Richmond. Drs. R. Finley Gayle and O. B. Darden of Richmond and Dr. Frank H. Redwood of Norfolk were named as new members of the executive committee. Doctors among the new directors are: Dr. David C. Wilson, Charlottesville; Drs. Beverley R. Tucker, Howard R. Masters and R. Finley Gayle of Richmond; Dr. Philip S. Smith, Abingdon; and Dr. Joseph E. Barrett, Marion.

Dr. Sidney Grey Page, Jr.

Has opened offices for the practice of internal medicine in the Medical Arts Building, Richmond, and will be associated with Dr. William H. Higgins. Dr. Page graduated from the Medical College of Virginia in 1938 and, for the past two years, has been on the Medical House Staff of Peter Bent Brigham Hospital in Boston, Mass.

American Public Health Association.

At the annual meeting held in Detroit the week of October 7, Dr. W. S. Leathers, Nashville, Tenn., succeeded to the presidency. Dr. John L. Rice, New York City, was named president-elect; and Dr. Reginald M. Atwater, New York City, was continued as executive secretary. The 70th annual meeting will be held in Atlantic City, N. J., in October, 1941.

C. & O. Surgeons.

The annual meeting of the C. & O. Railway Surgeons Association was held November 8-9, with Dr. M. J. Payne, President, Staunton, presiding. New officers elected are president, Dr. Clarence Porter Jones, Newport News, and vice-president, Dr. Thos. W. Moore, Huntington, W. Va.

Dr. Albert G. Schnurman

Is now located at Radford, where he is employed by Mason and Hagan Company, who are engaged in constructing a powder plant for the Hercules Powder Company. He is a graduate of the University of Virginia, Department of Medicine, in 1938, following which he interned at Sinai Hospital, Baltimore. Dr. Schnurman was recently resident physician at the Roanoke Hospital, Roanoke.

Post-Graduate Course in Ophthalmology and Otolaryngology.

The seventh post-graduate course in these specialties will be held at the University of Virginia, December 10th-13th, inclusive, in the amphitheater and operating rooms of the University of Virginia which is sponsoring the lectures and clinics. The fee for this course is $25.00 for the full course or $15.00 for either part. Further information and

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program may be secured from Dr. Fletcher D. Woodward, Box 1685, University Station, Charlottesville, Va.

Dr. H. I. Pifer

Of Winchester, member of the class of '21, Medical College of Virginia, received his fellowship into the American College of Surgeons, at the recent meeting in Chicago.

Dr. Waverly R. Payne

Of Newport News, was the guest speaker before the Section on Obstetrics of the Norfolk County Medical Society, at its meeting on November 25th, his subject being Cesarean Section with Special Reference to the Lower Segment Operation; Report of 110 Consecutive Cases. Lantern slides were shown.

Attend American Academy of Pediatrics.

At the meeting of the Academy in Memphis, November 18th and 19th, the following Virginians were among those who registered attendance: Drs. Thomas D. Jones, W. Ambrose McGee and James B. Stone of Richmond, and Dr. Leta J. White of Petersburg.

To Head Pine Camp, Richmond.

Dr. George A. Welchons, for the past two years assistant director of Pine Camp, Richmond's tuberculosis hospital, has been appointed superintendent and medical director, effective December 1st, succeeding Dr. P. E. Schools who recently tendered his resignation after a service of fifteen years. Dr. Welchons is a native of Goochland County and a graduate of the Medical College of Virginia. Before becoming Dr. Schools' assistant in 1938, he was a member of the resident staff of the Hospital Division of the Medical College of Virginia.

Dr. Otis Whitlock,

Who has recently been located in Richmond, has returned to Powhatan where he will be engaged in general practice.

Dr. James H. Gordon,

Captain, U. S. A., has just been assigned to the medical service at Walter Reed General Hospital, Washington, for a year of extended active duty. He is an alumnus of the Medical College of Virginia, class of '34, and has recently been engaged in graduate work in venereal diseases at Stokes Clinic, University of Pennsylvania, Philadelphia.

Dr. C. H. Armentrout,

Formerly of Flint Hill, who recently completed a postgraduate course in internal medicine at Harvard University, has located in Arcade Building, Asheville, N. C., for the practice of his specialty.

Dr. Charles W. Scott,

Of the State Health Department, by invitation, spoke before the Sullivan-Johnson Medical Society of Tennessee, at Bristol Hotel, on November 6. His subject was "The Management of the Tuberculous Patient in the Home".

American Board of Obstetrics and Gynecology.

In accordance with its Articles of Incorporation, the American Board of Obstetrics and Gynecology has elected Dr. Norman F. Miller of Ann Arbor, Michigan, and Dr. Willard R. Cooke of Galveston, Texas, as members, directors, and examiners, to fill the unexpired terms of Dr. Jennings C. Litzenberg and Dr. Grandison D. Royston, both of whom resigned October 15, 1940.

The written examination and review of case histories (Part I) for Group B candidates will be held in the various cities of the United States and Canada on Saturday, January 4, 1941, at 2:00 P. M. Formal notice of the place of examination will be sent each candidate several weeks in advance of the examination date. Candidates who successfully complete the Part I examination proceed automatically to the Part II examintion to be held in June, 1941.

Application for admission to Group A (Part II), examinations must be on file in the Secretary's Office not later than March 15, 1941.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

New Books.

The following are recent acquisitions to the Library of the Medical College of Virginia and are available to our readers, the only cost being return postage.

Menkin, V.—Dynamics of inflammation.
Metchnikoff, E.—Founders of modern medicine.
Moller-Christensen, V.—The history of the forceps.
Morton, R. S.—A doctor's holiday in Iran.
Packard, E. et als.—Artificial pneumothorax.
Pancoast, H. K. et als.—The head and neck in roentgen diagnosis.

Randell, M.—Training for childbirth.
Roeder, H.—Atlas of cardio-roentgenology.
Schnitker, M.A.—Sulfanilamide, sulfapyridine and allied compounds.
Sheldon, W. H.—The varieties of human physique.
Tidy, H. L.—A synopsis of medicine.
Trueta, J.—Treatment of war wounds and fractures.
Vaughan, W. T.—Primer of allergy.
Wilder, R. M.—Clinical diabetes mellitus and hyperinsulinism.
Wilson, M. G.—Rheumatic fever.
Zinsser, H.—As I remember him.

Lieut.-Comdr. J. F. Terrell (MC), U. S. N.,

Who has been stationed at Honolulu, T. H., is now at the U. S. Naval Training Station, Newport, R. I. He is an alumnus of the Medical College of Virginia.

Dr. T. J. Hughes,

Roanoke, has been elected to membership in the International College of Surgeons. He will be received at the next international convocation in Mexico City in August, 1941.

For Sale—

Drug store, established and operated for years by physician in connection with his practice. Doctor now deceased. Store being operated and doing good business. Located in town of 800, fifty miles from Richmond. Wonderful opening for doctor to operate store and practice. Must have $1,000 cash; balance monthly. Store is modern and well arranged for doctor's office in store. Address "Drug Store" care this JOURNAL. (*Adv.*)

Resident Physician Wanted—

For 72-bed fully equipped hospital. Work predominantly surgical. $100.00 per month and complete maintenance. Appointment immediate. Address Petersburg Hospital, Petersburg, Va. (*Adv.*)

For Rent—

Doctor's office, fully equipped, in the town of Leesburg, Virginia. Good opportunity for a practicing physician. Write Mrs. H. P. Gibson, Leesburg, Va. (*Adv.*)

Obituary Record

Dr. John Shelton Horsley, Jr.

The announcement that this brilliant young surgeon of Richmond was instantly killed in an automobile accident on November 22nd will bring sorrow to many who admired him for his personality as well as medical skill. He was born in El Paso, Texas, nearly forty-one years ago, when his father was in charge of a hospital there, but came to Virginia a few years later and had since made his home here. Upon completing his pre-medical course at the University of Virginia, he entered Harvard Medical School from which he graduated in 1922, later doing post-graduate work at the University of Chicago, and taking special surgical work at Mayo Clinic. Dr. Horsley became associated with his father at St. Elizabeth's Hospital in 1923 and specialized in general and plastic surgery. At the time of his death, he was associate professor of surgery at the Medical College of Virginia and associate surgeon for its hospitals, and plastic surgeon at Crippled Children's Hospital, in addition to many other activities. He was identified with a large number of medical organizations in all of which he was an interested member. Besides his wife and three children, he is survived by his parents and several brothers and sisters.

Dr. Joseph Thomas Buxton,

Prominent Newport News surgeon and founder of the Elizabeth Buxton Hospital, died November 5, having been in ill health for some years. He was a native of North Carolina and sixty-five years of age. Dr. Buxton received his medical degree from the University of Pennsylvania in 1897. He had been an active member of the Medical Society of Virginia since 1902, having served as a vice-president and on various committees. Dr. Buxton founded the Elizabeth Buxton Hospital in 1899, and, although he had retired from active practice, he continued to hold the post of surgeon. Two daughters and three sons, one of them Dr. Russell von Lehn Buxton of Newport News, survive him.

Dr. John Gilmer Reynolds,

Well-known physician of Chatham, died October 25, after an illness of several weeks. He was seventy-one years of age and a graduate of the former Hospital College of Medicine, Louisville, Ky., in 1904. Dr. Reynolds had been a member of the Medical Society of Virginia for eighteen years. His wife and a daughter survive him.

Dr. Enoch Wilson Baxter,

Moyock, N. C., died on August 10, at the age of seventy-nine. Dr. Baxter graduated from the College

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of Physicians and Surgeons of Baltimore in 1887 and practiced for a number of years in Norfolk, before retiring and returning to his native State several years ago. He had been a member of the Medical Society of Virginia for over fifty years.

Dr. David Wendell Eames,

Chief of the medical service of the Kecoughtan Veterans Administration, died unexpectedly at his home in Elizabeth City County on November 8. He was fifty-four years of age and a graduate of the former University of the South, Sewanee, Tenn., in 1908. Dr. Eames was a member of the Hampton Rotary Club, the Elks, Masons, and other organizations. His wife survives him.

Dr. William Goggin Crockett,

Professor of pharmacy at the Medical College of Virginia, Richmond, died October 29, following a heart attack. He was a former president of the American Association of Colleges of Pharmacy and a member of numerous other pharmaceutical and chemical associations. Dr. Crockett had been with the Medical College of Virginia since 1920.

Dr. Samuel S. Guerrant,

Callaway, died October 28, after an illness of several days. He was seventy-three years of age and a graduate of Tulane University in 1891, but practiced medicine for only a short time. For some years he had devoted a great deal of time to horticulture, having perfected apple strains that have become nationally known.

Dr. George Tapscott Snead,

An alumnus of the Medical College of Virginia, class of '80, died at his home in Princess Anne County, Va., October 30. He practiced medicine for about fifteen years, after which he represented his section in the State Legislature, which position he held until he was forced to retire because of his health.

Lt. Col. Robert Baylor Shackelford,

Retired surgeon, U. S. Army, died November 2, at his home near Cismont, after an illness of about a month. He was a native of Albemarle County and fifty-nine years of age. He graduated in medicine from the University of Virginia in 1909, and practiced for a time in Prince William County before entering the Army. His wife and a daughter survive him.

Dr. John P. Munroe,

Charlotte, N. C., died on October 14th, at the age of 83 years, death being due to pneumonia. He was a graduate of the University of Virginia, Department of Medicine in 1885, and well known in this State. He was formerly professor of neurology and practice of medicine in the North Carolina Medical College.

Resolutions on Dr. Watson.

At the October meeting of the Roanoke Academy of Medicine, the following resolutions were adopted:

Dr. Everett Watson was born at Hillsville, Virginia, August 16, 1888.

He came to Roanoke at the age of five, attended Roanoke schools, grading from Roanoke High School, 1908.

He was graduated from the University College of Medicine, Richmond, Virginia, in 1912.

Dr. Watson spent one year as patient and House Physician at Mountain View Sanatorium, Catawba, Virginia, and, deciding to make his life work the treatment of tuberculosis, he spent the next year at Saranac Lake.

Coming back to Roanoke in 1915, he organized, built, and operated Mount Regis Tuberculosis Sanatorium in Roanoke County until the year of his death.

A constant sufferer from the disease he made it his life's work to fight, he fought bravely on and on, overcoming seemingly insuperable obstacles.

By his untiring zeal he made Mount Regis one of the best-known institutions of its kind in the State, drawing patients from all over the South, and endeared himself to thousands of patients and physicians who came to him for treatment and consultation.

It may be truly said of him: "This loving husband, father, and friend passed from life where manhood's morning almost touches noon, and while the shadows were still falling toward the west".

Loving all and loved by all, he has left only the sweetest memories to be long cherished by a multitude of friends.

The Roanoke Academy of Medicine extends to his family and friends its sincerest sympathy in their bereavement.

G. M. MAXWELL, M. D., *Chairman*
CHURCHILL ROBERTSON, M. D.
J. B. NICHOLLS, M. D.
Committee.

End

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